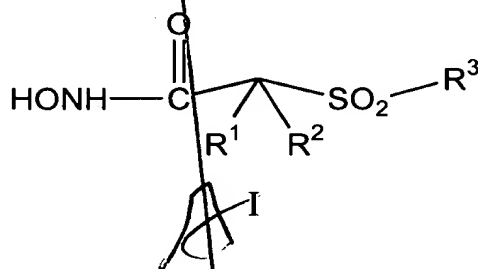


WHAT IS CLAIMED:

1. A process for treating a host mammal having a condition associated with pathological matrix metalloprotease (MMP) activity that comprises administering a metalloprotease inhibitor compound or a pharmaceutically acceptable salt thereof in an effective amount to a mammalian host having such a condition, said metalloprotease inhibitor inhibiting the activity of one or more of MMP-2, MMP-9 and MMP-13, while exhibiting substantially less inhibitory activity against MMP-1, said compound corresponding in structure to formula (I), below



wherein

R<sup>1</sup> and R<sup>2</sup> are both hydrido or R<sup>1</sup> and R<sup>2</sup> together with the atoms to which they are bonded form a 5- to 8-membered ring containing one, two or three heteroatoms in the ring that are oxygen, sulfur or nitrogen;

R<sup>3</sup> is an optionally substituted aryl or optionally substituted heteroaryl radical, and when said aryl or heteroaryl radical is substituted, the substituent is (a) selected from the group consisting of an optionally substituted cycloalkyl, heterocycloalkyl, aryl, heteroaryl, aralkyl, heteroaralkyl, aralkoxy, heteroaralkoxy, aralkoxyalkyl, aryloxyalkyl, aralkanoylalkyl,

arylcarbonylalkyl, aralkylaryl, aryloxyalkylaryl,  
aralkoxyaryl, arylazoaryl, arylhydrazinoaryl,  
alkylthioaryl, arylthioalkyl, alkylthioaralkyl,  
aralkylthioalkyl, an aralkylthioaryl radical, the  
5 sulfoxide or sulfone of any of the thio substituents,  
and a fused ring structure comprising two or more 5-  
or 6-membered rings selected from the group  
consisting of aryl, heteroaryl, cycloalkyl and  
heterocycloalkyl, and (b) is itself optionally  
10 substituted with one or more substituents  
independently selected from the group consisting of a  
cyano, perfluoroalkyl, trifluoromethoxy,  
trifluoromethylthio, haloalkyl, trifluoromethylalkyl,  
aralkoxycarbonyl, aryloxycarbonyl, hydroxy, halo,  
15 alkyl, alkoxy, nitro, thiol, hydroxycarbonyl,  
aryloxy, arylthio, aralkyl, aryl, arylcarbonylamino,  
heteroaryloxy, heteroarylthio, heteroaralkyl,  
cycloalkyl, heterocyclooxy, heterocyclothio,  
heterocycloamino, cycloalkyloxy, cycloalkylthio,  
20 heteroaralkoxy, heteroaralkylthio, aralkoxy,  
aralkylthio, aralkylamino, heterocyclo, heteroaryl,  
arylazo, hydroxycarbonylalkoxy, alkoxycarbonylalkoxy,  
alkanoyl, arylcarbonyl, aralkanoyl, alkanoyloxy,  
aralkanoyloxy, hydroxyalkyl, hydroxyalkoxy,  
25 alkylthio, alkoxyalkylthio, alkoxycarbonyl,  
aryloxyalkoxyaryl, arylthioalkylthioaryl,  
aryloxyalkylthioaryl, arylthioalkoxyaryl,  
hydroxycarbonylalkoxy, hydroxycarbonylalkylthio,  
alkoxycarbonylalkoxy, alkoxycarbonylalkylthio, amino,  
30 wherein the amino nitrogen is (i) unsubstituted,  
or (ii) substituted with one or two substituents  
that are independently selected from the group  
consisting of an alkyl, aryl, heteroaryl,

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aralkyl, cycloalkyl, aralkoxycarbonyl,  
alkoxycarbonyl, arylcarbonyl, aralkanoyl,  
heteroarylcarbonyl, heteroaralkanoyl and an  
alkanoyl group, or (iii) wherein the amino  
5 nitrogen and two substituents attached thereto  
form a 5- to 8-membered heterocyclo or  
heteroaryl ring containing zero to two  
additional heteroatoms that are nitrogen, oxygen  
or sulfur and which ring itself is (a)  
10 unsubstituted or (b) substituted with one or two  
groups independently selected from the group  
consisting of an aryl, alkyl, heteroaryl,  
aralkyl, heteroaralkyl, hydroxy, alkoxy,  
alkanoyl, cycloalkyl, heterocycloalkyl,  
15 alkoxycarbonyl, hydroxyalkyl, trifluoromethyl,  
benzofused heterocycloalkyl, hydroxyalkoxyalkyl,  
aralkoxycarbonyl, hydroxycarbonyl,  
aryloxycarbonyl, benzofused heterocycloalkoxy,  
benzofused cycloalkylcarbonyl, heterocyclo-  
20 alkylcarbonyl, and a cycloalkylcarbonyl group,  
carbonylamino

wherein the carbonylamino nitrogen is (i)  
unsubstituted, or (ii) is the reacted amine of  
an amino acid, or (iii) substituted with one or  
25 two radicals selected from the group consisting  
of an alkyl, hydroxyalkyl, hydroxyheteroaralkyl,  
cycloalkyl, aralkyl, trifluoromethylalkyl,  
heterocycloalkyl, benzofused heterocycloalkyl,  
benzofused heterocycloalkyl, benzofused  
30 cycloalkyl, and an N,N-dialkylsubstituted  
alkylamino-alkyl group, or (iv) the carboxamido  
nitrogen and two substituents bonded thereto  
together form a 5- to 8-membered heterocyclo,

heteroaryl or benzofused heterocycloalkyl ring  
that is itself unsubstituted or substituted with  
one or two radicals independently selected from  
the group consisting of an alkyl,  
5 alkoxy carbonyl, nitro, heterocycloalkyl,  
hydroxy, hydroxy carbonyl, aryl, aralkyl,  
heteroaralkyl and an amino group,

wherein the amino nitrogen is

(i) unsubstituted, or (ii) substituted with  
10 one or two substituents that are  
independently selected from the group  
consisting of alkyl, aryl, and heteroaryl,  
or (iii) wherein the amino nitrogen and two  
substituents attached thereto form a 5- to  
15 8-membered heterocyclo or heteroaryl ring,  
and an aminoalkyl group

wherein the aminoalkyl nitrogen is (i)  
unsubstituted, or (ii) substituted with one or two  
substituents independently selected from the group  
20 consisting of an alkyl, aryl, aralkyl, cycloalkyl,  
aralkoxy carbonyl, alkoxy carbonyl, and an alkanoyl  
group, or (iii) wherein the aminoalkyl nitrogen and  
two substituents attached thereto form a 5- to 8-  
membered heterocyclo or heteroaryl ring.

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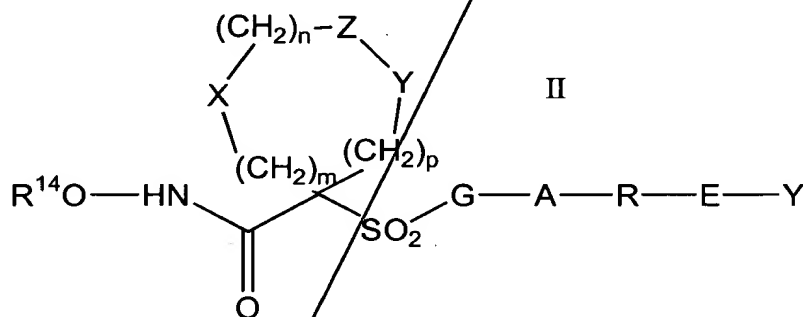
2. The process according to claim 1  
wherein  $R^1$  and  $R^2$  together with the atoms to which  
they are bonded form a 5- to 8-membered ring  
containing one, two or three heteroatoms in the ring  
30 that are oxygen, sulfur or nitrogen;

3. The process according to claim 2  
wherein  $R^3$  is a single-ringed aryl or heteroaryl  
group that is 5- or 6-membered, and is itself  
substituted at its own 4-position when a 6-membered  
5 ring or at its own 3- or 4-position when a 5-membered  
ring with a substituent selected from the group  
consisting of one other single-ringed aryl or  
heteroaryl group, a  $C_3$ - $C_{14}$  alkyl group, a N-piperidyl  
group, a N-piperazinyl group, a phenoxy group, a  
10 thiophenoxy group, a 4-thiopyridyl group, a phenylazo  
group and a benzamido group.

4. The process according to claim 3  
wherein  $R^3$  contains two or more 5- or 6-membered  
15 rings.

5. The process according to claim 3  
wherein  $R^3$ , when rotated about an axis drawn through  
the  $SO_2$ -bonded 1-position and the substituent-bonded  
20 4-position of a 6-membered ring or the  $SO_2$ -bonded 1-  
position and substituent-bonded 3- or 4-position of a  
5-membered ring, defines a three-dimensional volume  
whose widest dimension has the width in a direction  
transverse to that axis to rotation of about one  
25 furanyl ring to about two phenyl rings.

6. The process according to claim 3  
wherein  $R^3$  has a length that is greater than that of  
a pentyl group and a length that is less than that of  
30 an icosyl group.

[illegible]

15                    wherein

R<sup>14</sup> is hydrido, a pharmaceutically acceptable cation or C(W)R<sup>15</sup> where W is O or S and R<sup>15</sup> is selected from the group consisting of a C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, C<sub>1</sub>-C<sub>6</sub>-alkoxy, heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>3</sub>-C<sub>8</sub>-cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy, ar-C<sub>1</sub>-C<sub>6</sub>-alkoxy, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryl and amino C<sub>1</sub>-C<sub>6</sub>-alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two substituents independently selected from the group consisting of an C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl,

C<sub>3</sub>-C<sub>8</sub>-cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, ar-C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonyl, and C<sub>1</sub>-C<sub>6</sub>-alkanoyl radical, or (iii) wherein the amino C<sub>1</sub>-C<sub>6</sub>-alkyl nitrogen and two substituents attached thereto  
5 form a 5- to 8-membered heterocyclo or heteroaryl ring;

m is zero, 1 or 2;

n is zero, 1 or 2;

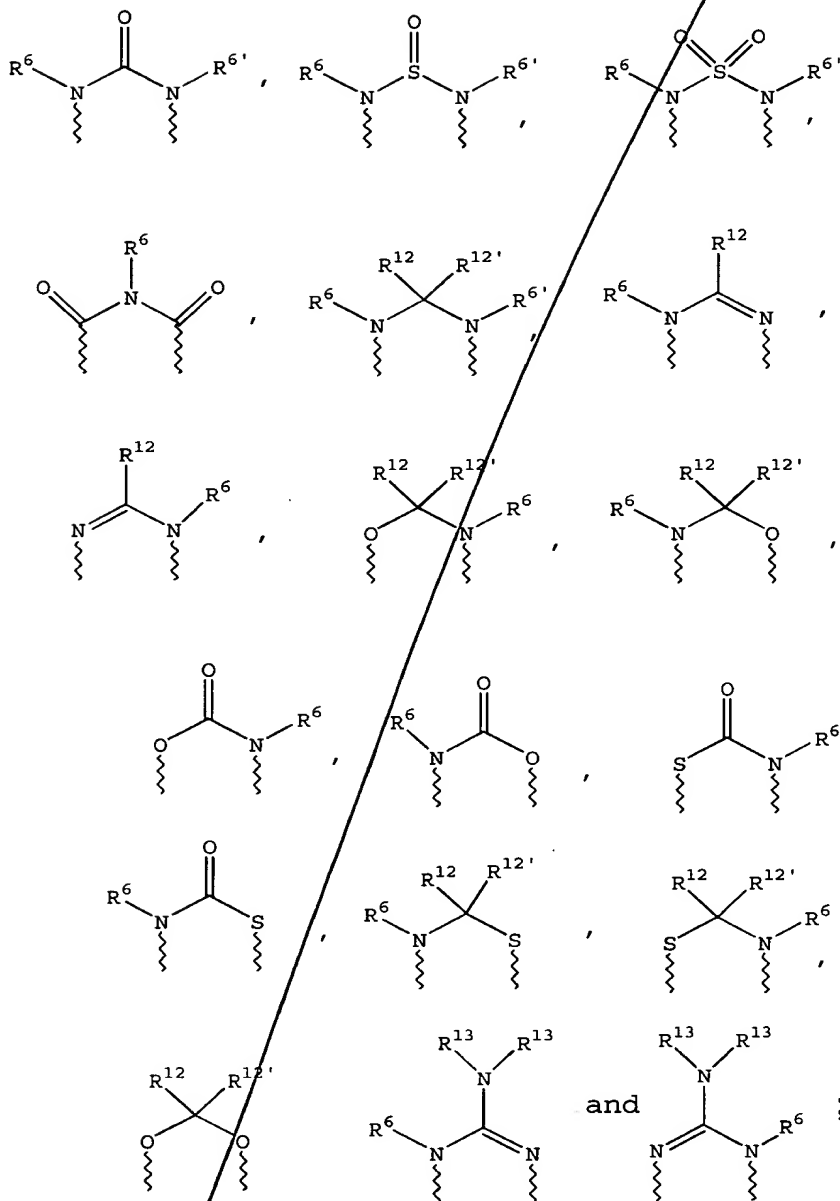
p is zero, 1 or 2;

10 the sum of m + n + p = 1, 2, 3 or 4;

(a) one of X, Y and Z is selected from the group consisting of C(O), NR<sup>6</sup>, O, S, S(O), S(O)<sub>2</sub> and NS(O)<sub>2</sub>R<sup>7</sup>, and the remaining two of X, Y and Z are CR<sup>8</sup>R<sup>9</sup>, and CR<sup>10</sup>R<sup>11</sup>, or

15 (b) X and Z or Z and Y together constitute a moiety that is selected from the group consisting of NR<sup>6</sup>C(O), NR<sup>6</sup>S(O), NR<sup>6</sup>S(O)<sub>2</sub>, NR<sup>6</sup>S, NR<sup>6</sup>O, SS, NR<sup>6</sup>NR<sup>6</sup> and OC(O), with the remaining one of X, Y and Z being CR<sup>8</sup>R<sup>9</sup>, or

20 (c) n is zero and X, Y and Z together constitute a moiety selected from the group consisting of



5                    wherein wavy lines are bonds to the atoms  
of the depicted ring;

                  R<sup>6</sup> and R<sup>6'</sup> are independently selected from  
the group consisting of hydrido, formyl, sulfonic-C<sub>1</sub>-  
C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl,  
10    hydroxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl-C<sub>1</sub>-  
C<sub>6</sub>-alkyl, R<sup>8</sup>R<sup>9</sup>-aminocarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-



- alkoxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl, hydroxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonylcarbonyl, hydroxycarbonylcarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkylcarbonylcarbonyl,
- 5 R<sup>8</sup>R<sup>9</sup>-aminocarbonylcarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkanoyl, aryl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aroyl, bis(C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl)-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-haloalkyl, C<sub>1</sub>-C<sub>6</sub>-perfluoroalkyl, C<sub>1</sub>-C<sub>6</sub>-trifluoromethylalkyl, C<sub>1</sub>-C<sub>6</sub>-perfluoroalkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-
- 10 alkyl, C<sub>3</sub>-C<sub>6</sub>-cycloalkyl, heteroarycarbonyl, heterocyclocarbonyl, C<sub>3</sub>-C<sub>8</sub>-heterocycloalkyl, C<sub>3</sub>-C<sub>8</sub>-heterocycloalkylcarbonyl, aryl, C<sub>5</sub>-C<sub>6</sub>-heterocyclo, C<sub>5</sub>-C<sub>6</sub>-heteroaryl, C<sub>3</sub>-C<sub>8</sub>-cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl,
- 15 heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroarylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, arylsulfonyl, C<sub>1</sub>-C<sub>6</sub>-alkylsulfonyl, C<sub>5</sub>-C<sub>6</sub>-heteroarylsulfonyl, carboxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>4</sub>-alkoxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aminocarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkyl(R<sup>8</sup>N)iminocarbonyl, aryl(R<sup>8</sup>N)iminocarbonyl, C<sub>5</sub>-
- 20 C<sub>6</sub>-heterocyclo(R<sup>8</sup>N)iminocarbonyl, arylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, arylthio-C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>1</sub>-C<sub>4</sub>-alkylthio-C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>5</sub>-C<sub>6</sub>-heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkyl, halo-C<sub>1</sub>-C<sub>6</sub>-alkanoyl, hydroxy-C<sub>1</sub>-C<sub>6</sub>-alkanoyl, thiol-C<sub>1</sub>-C<sub>6</sub>-alkanoyl, C<sub>3</sub>-C<sub>6</sub>-alkenyl,
- 25 C<sub>3</sub>-C<sub>6</sub>-alkynyl, C<sub>1</sub>-C<sub>4</sub>-alkoxy-C<sub>1</sub>-C<sub>4</sub>-alkyl, C<sub>1</sub>-C<sub>5</sub>-alkoxycarbonyl, aryloxycarbonyl, NR<sup>8</sup>R<sup>9</sup>-(R<sup>8</sup>)iminomethyl, NR<sup>8</sup>R<sup>9</sup>-C<sub>1</sub>-C<sub>5</sub>-alkylcarbonyl, hydroxy-

C<sub>1</sub>-C<sub>5</sub>-alkyl, R<sup>8</sup>R<sup>9</sup>-aminocarbonyl, R<sup>8</sup>R<sup>9</sup>-aminocarbonyl-  
C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl, hydroxyaminocarbonyl, R<sup>8</sup>R<sup>9</sup>-  
aminosulfonyl, R<sup>8</sup>R<sup>9</sup>-aminosulfon-C<sub>1</sub>-C<sub>6</sub>-alkyl, R<sup>8</sup>R<sup>9</sup>-  
amino-C<sub>1</sub>-C<sub>6</sub>-alkylsulfonyl and an R<sup>8</sup>R<sup>9</sup>-amino-C<sub>1</sub>-C<sub>6</sub>-  
5 alkyl group;

R<sup>7</sup> is selected from the group consisting of  
a arylalkyl, aryl, heteroaryl, heterocyclo, C<sub>1</sub>-C<sub>6</sub>-  
alkyl, C<sub>3</sub>-C<sub>6</sub>-alkynyl, C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>1</sub>-C<sub>6</sub>-  
carboxyalkyl and a C<sub>1</sub>-C<sub>6</sub>-hydroxyalkyl group;

10 R<sup>8</sup> and R<sup>9</sup> and R<sup>10</sup> and R<sup>11</sup> are independently  
selected from the group consisting of a hydrido,  
hydroxy, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkanoyl, aroyl, aryl,  
ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryl, heteroar-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>2</sub>-  
C<sub>6</sub>-alkynyl, C<sub>2</sub>-C<sub>6</sub>-alkenyl, thiol-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-  
15 alkylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, cycloalkyl, cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-  
alkyl, heterocycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-  
C<sub>6</sub>-alkyl, aralkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-  
alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxy-C<sub>1</sub>-C<sub>6</sub>-alkyl,  
hydroxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxycarbonylar-C<sub>1</sub>-C<sub>6</sub>-  
20 alkyl, aminocarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-  
alkyl, heteroaryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, arylthio-C<sub>1</sub>-C<sub>6</sub>-  
alkyl, heteroarylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, the sulfoxide or  
sulfone of any said thio substituents, perfluoro-C<sub>1</sub>-  
C<sub>6</sub>-alkyl, trifluoromethyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, halo-C<sub>1</sub>-C<sub>6</sub>-  
25 alkyl, alkoxycarbonylamino-C<sub>1</sub>-C<sub>6</sub>-alkyl and an amino-  
C<sub>1</sub>-C<sub>6</sub>-alkyl group wherein the aminoalkyl nitrogen is  
(i) unsubstituted or (ii) substituted with one or two

radicals independently selected from the group consisting of C<sub>1</sub>-C<sub>6</sub>-alkyl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, cycloalkyl and C<sub>1</sub>-C<sub>6</sub>-alkanoyl, or wherein R<sup>8</sup> and R<sup>9</sup> or R<sup>10</sup> and R<sup>11</sup> and the carbon to which they are bonded form a carbonyl group, or wherein R<sup>8</sup> and R<sup>9</sup> or R<sup>10</sup> and R<sup>11</sup>,  
5 or R<sup>8</sup> and R<sup>10</sup> together with the atoms to which they are bonded form a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclic or heteroaryl ring containing one or two heteroatoms that are nitrogen,  
10 oxygen, or sulfur, with the proviso that only one of R<sup>8</sup> and R<sup>9</sup> or R<sup>10</sup> and R<sup>11</sup> is hydroxy;

R<sup>12</sup> and R<sup>12'</sup> are independently selected from the group consisting of a hydrido, C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryl, heteroaralkyl, C<sub>2</sub>-  
15 C<sub>6</sub>-alkynyl, C<sub>2</sub>-C<sub>6</sub>-alkenyl, thiol-C<sub>1</sub>-C<sub>6</sub>-alkyl, cycloalkyl, cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, heterocycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, amino-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxycarbonyl-C<sub>1</sub>-  
20 C<sub>6</sub>-alkyl, hydroxycarbonylar-C<sub>1</sub>-C<sub>6</sub>-alkyl, aminocarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, arylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroarylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, the sulfoxide or sulfone of any said thio  
25 substituents, perfluoro-C<sub>1</sub>-C<sub>6</sub>-alkyl, trifluoromethyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, halo-C<sub>1</sub>-C<sub>6</sub>-alkyl, alkoxycarbonylamino-C<sub>1</sub>-C<sub>6</sub>-alkyl and an amino-C<sub>1</sub>-C<sub>6</sub>-alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii)

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substituted with one or two radicals independently selected from the group consisting of  $C_1-C_6$ -alkyl, ar- $C_1-C_6$ -alkyl, cycloalkyl and  $C_1-C_6$ -alkanoyl;

5  $R^{13}$  is selected from the group consisting of a hydrido, benzyl, phenyl,  $C_1-C_6$ -alkyl,  $C_2-C_6$ -alkynyl,  $C_2-C_6$ -alkenyl and a  $C_1-C_6$ -hydroxyalkyl group; and

10 G-A-R-E-Y is a substituent that has a length greater than that of a pentyl group has a length that is less than that of an icosyl group wherein

G is an aryl or heteroaryl group;

A is selected from the group consisting of

- 15 (1) -O-;
- (2) -S-;
- (3) -NR<sup>17</sup>-;
- (4) -CO-N(R<sup>17</sup>) or -N(R<sup>17</sup>)-CO-, wherein R<sup>17</sup> is hydrogen,  $C_1-C_4$ -alkyl, or phenyl;
- 20 (5) -CO-O- or -O-CO-;
- (6) -O-CO-O-;
- (7) -HC=CH-;
- (8) -NH-CO-NH-;
- (9) -C≡C-;
- 25 (10) -NH-CO-O- or -O-CO-NH-;
- (11) -N=N-;
- (12) -NH-NH-; and
- (13) -CS-N(R<sup>18</sup>)- or -N(R<sup>18</sup>)-CS-, wherein R<sup>18</sup> is hydrogen  $C_1-C_4$ -alkyl, or phenyl; or

(14) A is absent and G is bonded directly to R;

R is a moiety selected from the group consisting of alkyl, alkoxyalkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, aralkyl, heteroaralkyl, heterocycloalkylalkyl, cycloalkylalkyl, cycloalkoxyalkyl, heterocycloalkoxyalkyl, aryloxyalkyl, heteroaryloxyalkyl, arylthioalkyl, heteroarylthioalkyl, cycloalkylthioalkyl, and a heterocycloalkylthioalkyl group wherein the aryl or heteroaryl or cycloalkyl or heterocycloalkyl substituent is (i) unsubstituted or (ii) substituted with one or two radicals selected from the group consisting of a halo, alkyl, perfluoroalkyl, perfluoroalkoxy, perfluoroalkylthio, trifluoromethylalkyl, amino, alkoxycarbonylalkyl, alkoxy, C<sub>1</sub>-C<sub>2</sub>-alkylene-dioxy, hydroxycarbonylalkyl, hydroxycarbonylalkylamino, nitro, hydroxy, hydroxyalkyl, alkanoylamino, and a alkoxycarbonyl group, and R is other than alkyl or alkoxyalkyl when A is -O- or -S-;

E is selected from the group consisting of

- (1) -CO(R<sup>19</sup>)- or -(R<sup>19</sup>)CO-, wherein R<sup>19</sup> is a heterocycloalkyl, or a cycloalkyl group;
- (2) -CONH- or -HNCO-; and
- (3) -CO-;
- (4) -SO<sub>2</sub>-R<sup>19</sup>- or -R<sup>19</sup>-SO<sub>2</sub>-;
- (5) -SO<sub>2</sub>-;
- (6) -NH-SO<sub>2</sub>- or -SO<sub>2</sub>-NH-; or

(7) E is absent and R is bonded directly to Y; and

Y is absent or is selected from the group consisting of a hydrido, alkyl, alkoxy, haloalkyl, aryl, aralkyl, cycloalkyl, heteroaryl, hydroxy, aryloxy, aralkoxy, heteroaryloxy, heteroaralkyl, perfluoroalkoxy, perfluoroalkylthio, trifluoromethylalkyl, alkenyl, heterocycloalkyl, cycloalkyl, trifluoromethyl, alkoxycarbonyl, and a aminoalkyl group, wherein the aryl or heteroaryl or heterocycloalkyl group is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of an alkanoyl, halo, nitro, aralkyl, aryl, alkoxy, and an amino group wherein the amino nitrogen is (i) unsubstituted or (ii) substituted with one or two groups independently selected from hydrido, alkyl, and an aralkyl group.

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~~8. The process according to claim 7~~

wherein said -G-A-R-E-Y substituent contains two to four carbocyclic or heterocyclic rings.

9. The process according to claim 8

wherein each of the two to four rings is 6-membered.

10. The process according to claim 7

wherein said -G-A-R-E-Y substituent has a length that is greater than a hexyl group and a length that is less than that of a stearyl group.

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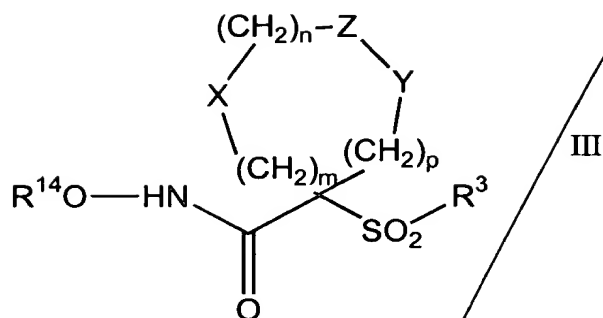
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15. A process for treating a host mammal having a condition associated with pathological matrix metalloprotease (MMP) activity that comprises administering a metalloprotease inhibitor compound or a pharmaceutically acceptable salt thereof in an effective amount to a mammalian host having such a condition, said metalloprotease inhibitor inhibiting the activity of one or more of MMP-2, MMP-9 and MMP-13, while exhibiting substantially less inhibitory activity against MMP-1, said compound corresponding in structure to formula III, below



wherein

$R^3$  is a single-ringed aryl or heteroaryl group that is 5- or 6-membered, and is itself substituted at its own 4-position when a 6-membered ring and at its own 3- or 4-position when a 5-membered ring with a substituent selected from the group consisting of a thiophenoxy, 4-chloro-phenoxy, 3-chlorophenoxy, 4-methoxyphenoxy, 3-benzodioxol-5-yloxy, 3,4-dimethylphenoxy, 4-fluorophenoxy, 4-fluorothiophenoxy, phenoxy, 4-trifluoromethoxyphenoxy, 4-trifluoromethylphenoxy, 4-(trifluoromethylthio)phenoxy, 4-(trifluoromethylthio)thiophenoxy, 4-chloro-3-fluorophenoxy, 4-isopropoxyphenoxy, 4-isopropylphenoxy, (2-methyl-1,3-benzothiazol-5-yl)oxy, 4-(1H-imidazol-1-yl)phenoxy, 4-chloro-3-methylphenoxy, 3-methyl-phenoxy, 4-ethoxyphenoxy, 3,4-difluorophenoxy, 4-chloro-3-methylphenoxy, 4-fluoro-3-chlorophenoxy, 4-(1H-1,2,4-triazol-1-yl)phenoxy, 3,5-difluorophenoxy, 3,4-dichlorophenoxy, 4-cyclopentylphenoxy, 4-bromo-3-methylphenoxy, 4-bromophenoxy, 4-methylthiophenoxy, 4-phenylphenoxy, 4-benzylphenoxy, 6-quinolinyloxy, 4-amino-3-methylphenoxy, 3-methoxyphenoxy, 5,6,7,8-tetrahydro-2-naphthalenyloxy, 3-hydroxymethylphenoxy, and a 4-benzyloxyphenoxy group;



5  $R^{14}$  is hydrido, a pharmaceutically acceptable cation or  $C(W)R^{15}$  where W is O or S and  $R^{15}$  is selected from the group consisting of a  $C_1$ - $C_6$ -alkyl, aryl,  $C_1$ - $C_6$ -alkoxy, heteroaryl- $C_1$ - $C_6$ -alkyl,  $C_3$ - $C_8$ -cycloalkyl- $C_1$ - $C_6$ -alkyl, aryloxy, ar- $C_1$ - $C_6$ -alkoxy, ar- $C_1$ - $C_6$ -alkyl, heteroaryl and amino  $C_1$ - $C_6$ -alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two substituents independently selected from the group consisting of an  $C_1$ - $C_6$ -alkyl, aryl, ar- $C_1$ - $C_6$ -alkyl,  $C_3$ - $C_8$ -cycloalkyl- $C_1$ - $C_6$ -alkyl, ar- $C_1$ - $C_6$ -alkoxycarbonyl,  $C_1$ - $C_6$ -alkoxycarbonyl, and  $C_1$ - $C_6$ -alkanoyl radical, or (iii) wherein the amino  $C_1$ - $C_6$ -alkyl nitrogen and two substituents attached thereto form a 5- to 8-membered heterocyclo or heteroaryl ring;

m is zero, 1 or 2;

n is zero, 1 or 2;

p is zero, 1 or 2;

20 the sum of  $m + n + p = 1, 2, 3$  or 4;

(a) one of X, Y and Z is selected from the group consisting of  $C(O)$ ,  $NR^6$ , O, S,  $S(O)$ ,  $S(O)_2$  and  $NS(O)_2R^7$ , and the remaining two of X, Y and Z are  $CR^8R^9$ , and  $CR^{10}R^{11}$ , or

25 (b) X and Z or Z and Y together constitute a moiety that is selected from the group consisting of  $NR^6C(O)$ ,  $NR^6S(O)$ ,  $NR^6S(O)_2$ ,  $NR^6S$ ,  $NR^6O$ , SS,  $NR^6NR^6$  and  $OC(O)$ , with the remaining one of X, Y and Z being  $CR^8R^9$ , or

5



wherein wavy lines are bonds to the atoms  
of the depicted ring;

$R^6$  and  $R^{6'}$  are independently selected from the group consisting of hydrido, formyl, sulfonic- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkoxycarbonyl- $C_1$ - $C_6$ -alkyl, hydroxycarbonyl- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkylcarbonyl- $C_1$ - $C_6$ -alkyl,  $R^8R^9$ -aminocarbonyl- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkoxycarbonyl- $C_1$ - $C_6$ -alkylcarbonyl, hydroxycarbonyl- $C_1$ - $C_6$ -alkylcarbonyl,  $C_1$ - $C_6$ -alkylcarbonyl- $C_1$ - $C_6$ -alkylcarbonyl,  $C_1$ - $C_6$ -alkoxycarbonylcarbonyl, hydroxycarbonylcarbonyl,  $C_1$ - $C_6$ -alkylcarbonylcarbonyl,  $R^8R^9$ -aminocarbonylcarbonyl,  $C_1$ - $C_6$ -alkanoyl, aryl- $C_1$ - $C_6$ -alkyl, aroyl, bis( $C_1$ - $C_6$ -alkoxy- $C_1$ - $C_6$ -alkyl)- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -haloalkyl,  $C_1$ - $C_6$ -perfluoroalkyl,  $C_1$ - $C_6$ -trifluoromethylalkyl,  $C_1$ - $C_6$ -perfluoroalkoxy- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkoxy- $C_1$ - $C_6$ -alkyl,  $C_3$ - $C_6$ -cycloalkyl, heteroarycarbonyl, heterocyclocarbonyl,  $C_3$ - $C_8$ -heterocycloalkyl,  $C_3$ - $C_8$ -heterocycloalkylcarbonyl, aryl,  $C_5$ - $C_6$ -heterocyclo,  $C_5$ - $C_6$ -heteroaryl,  $C_3$ - $C_8$ -cycloalkyl- $C_1$ - $C_6$ -alkyl, aryloxy- $C_1$ - $C_6$ -alkyl, heteroaryloxy- $C_1$ - $C_6$ -alkyl, heteroaryl- $C_1$ - $C_6$ -alkoxy- $C_1$ - $C_6$ -alkyl, heteroarylthio- $C_1$ - $C_6$ -alkyl, arylsulfonyl,  $C_1$ - $C_6$ -alkylsulfonyl,  $C_5$ - $C_6$ -heteroarylsulfonyl, carboxy- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_4$ -alkoxycarbonyl- $C_1$ - $C_6$ -alkyl, aminocarbonyl,  $C_1$ - $C_6$ -alkyl( $R^8N$ )iminocarbonyl, aryl( $R^8N$ )iminocarbonyl,  $C_5$ - $C_6$ -heterocyclo( $R^8N$ )iminocarbonyl, arylthio- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkylthio- $C_1$ - $C_6$ -alkyl, arylthio- $C_3$ - $C_6$ -alkenyl,  $C_1$ - $C_4$ -alkylthio- $C_3$ - $C_6$ -alkenyl,  $C_5$ - $C_6$ -

heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkyl, halo-C<sub>1</sub>-C<sub>6</sub>-alkanoyl, hydroxy-C<sub>1</sub>-C<sub>6</sub>-alkanoyl, thiol-C<sub>1</sub>-C<sub>6</sub>-alkanoyl, C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>3</sub>-C<sub>6</sub>-alkynyl, C<sub>1</sub>-C<sub>4</sub>-alkoxy-C<sub>1</sub>-C<sub>4</sub>-alkyl, C<sub>1</sub>-C<sub>5</sub>-alkoxycarbonyl, aryloxycarbonyl, NR<sup>8</sup>R<sup>9</sup>-

- 5 (R<sup>8</sup>)iminomethyl, NR<sup>8</sup>R<sup>9</sup>-C<sub>1</sub>-C<sub>5</sub>-alkylcarbonyl, hydroxy-C<sub>1</sub>-C<sub>5</sub>-alkyl, R<sup>8</sup>R<sup>9</sup>-aminocarbonyl, R<sup>8</sup>R<sup>9</sup>-aminocarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl, hydroxyaminocarbonyl, R<sup>8</sup>R<sup>9</sup>-aminosulfonyl, R<sup>8</sup>R<sup>9</sup>-aminosulfon-C<sub>1</sub>-C<sub>6</sub>-alkyl, R<sup>8</sup>R<sup>9</sup>-amino-C<sub>1</sub>-C<sub>6</sub>-alkylsulfonyl and an R<sup>8</sup>R<sup>9</sup>-amino-C<sub>1</sub>-C<sub>6</sub>-alkyl group;
- 10

R<sup>7</sup> is selected from the group consisting of a arylalkyl, aryl, heteroaryl, heterocyclo, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub>-alkynyl, C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>1</sub>-C<sub>6</sub>-carboxyalkyl and a C<sub>1</sub>-C<sub>6</sub>-hydroxyalkyl group;

- 15 R<sup>8</sup> and R<sup>9</sup> and R<sup>10</sup> and R<sup>11</sup> are independently selected from the group consisting of a hydrido, hydroxy, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkanoyl, aroyl, aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryl, heteroar-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>2</sub>-C<sub>6</sub>-alkynyl, C<sub>2</sub>-C<sub>6</sub>-alkenyl, thiol-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, cycloalkyl, cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, heterocycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, aralkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxycarbonylar-C<sub>1</sub>-C<sub>6</sub>-alkyl, aminocarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, arylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroarylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, the sulfoxide or
- 20
- 25

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sulfone of any said thio substituents, perfluoro-C<sub>1</sub>-C<sub>6</sub>-alkyl, trifluoromethyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, halo-C<sub>1</sub>-C<sub>6</sub>-alkyl, alkoxycarbonylamino-C<sub>1</sub>-C<sub>6</sub>-alkyl and an amino-C<sub>1</sub>-C<sub>6</sub>-alkyl group wherein the aminoalkyl nitrogen is

5 (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C<sub>1</sub>-C<sub>6</sub>-alkyl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, cycloalkyl and C<sub>1</sub>-C<sub>6</sub>-alkanoyl, or wherein R<sup>8</sup> and R<sup>9</sup> or R<sup>10</sup> and R<sup>11</sup> and the carbon to which they are bonded form a

10 carbonyl group, or wherein R<sup>8</sup> and R<sup>9</sup> or R<sup>10</sup> and R<sup>11</sup>, or R<sup>8</sup> and R<sup>10</sup> together with the atoms to which they are bonded form a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclic or heteroaryl ring containing one or two heteroatoms that are nitrogen,

15 oxygen, or sulfur, with the proviso that only one of R<sup>8</sup> and R<sup>9</sup> or R<sup>10</sup> and R<sup>11</sup> is hydroxy;

R<sup>12</sup> and R<sup>12'</sup> are independently selected from the group consisting of a hydrido, C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryl, heteroaralkyl, C<sub>2</sub>-C<sub>6</sub>-alkynyl, C<sub>2</sub>-C<sub>6</sub>-alkenyl, thiol-C<sub>1</sub>-C<sub>6</sub>-alkyl,

20 cycloalkyl, cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, heterocycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, amino-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxycarbonylar-C<sub>1</sub>-C<sub>6</sub>-alkyl,

25 aminocarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, arylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroarylthio-C<sub>1</sub>-C<sub>6</sub>-

alkyl, the sulfoxide or sulfone of any said thio  
substituents, perfluoro-C<sub>1</sub>-C<sub>6</sub>-alkyl, trifluoromethyl-  
C<sub>1</sub>-C<sub>6</sub>-alkyl, halo-C<sub>1</sub>-C<sub>6</sub>-alkyl, alkoxycarbonylamino-  
C<sub>1</sub>-C<sub>6</sub>-alkyl and an amino-C<sub>1</sub>-C<sub>6</sub>-alkyl group wherein  
5 the aminoalkyl nitrogen is (i) unsubstituted or (ii)  
substituted with one or two radicals independently  
selected from the group consisting of C<sub>1</sub>-C<sub>6</sub>-alkyl,  
ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, cycloalkyl and C<sub>1</sub>-C<sub>6</sub>-alkanoyl; and

R<sup>13</sup> is selected from the group consisting  
10 of a hydrido, benzyl, phenyl, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>2</sub>-C<sub>6</sub>-  
alkynyl, C<sub>2</sub>-C<sub>6</sub>-alkenyl and a C<sub>1</sub>-C<sub>6</sub>-hydroxyalkyl  
group.

16. The process according to claim 15  
15 ~~wherein the sum of m + n + p = 1 or 2.~~

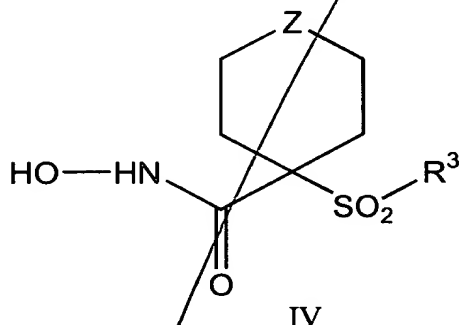
~~17. The process according to claim 15  
wherein Z is O, S or NR<sup>6</sup>.~~

20 18. The process according to claim 15  
wherein R<sup>6</sup> is selected from the group consisting of  
C<sub>3</sub>-C<sub>6</sub>-cycloalkyl, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>3</sub>-C<sub>6</sub>-  
alkynyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, amino-C<sub>1</sub>-C<sub>6</sub>-alkyl,  
aminosulfonyl, heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkyl,  
25 aryloxycarbonyl, and C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonyl.

19. The process according to claim 15  
wherein m = n = zero, p = 1, and Y is NR<sup>6</sup>.

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~~20. A process for treating a host mammal~~  
 having a condition associated with pathological  
 matrix metalloprotease (MMP) activity that comprises  
 administering a metalloprotease inhibitor compound or  
 5 a pharmaceutically acceptable salt thereof in an  
 effective amount to a mammalian host having such a  
 condition, said metalloprotease inhibitor inhibiting  
 the activity of one or more of MMP-2, MMP-9 and MMP-  
 13, while exhibiting substantially less inhibitory  
 10 activity against MMP-1, said compound corresponding  
 in structure to formula IV, below



wherein  $R^3$  is an optionally substituted  
 15 aryl or optionally substituted heteroaryl radical,  
 and when said aryl or heteroaryl radical is  
 substituted, the substituent is (a) selected from the  
 group consisting of an optionally substituted  
 cycloalkyl, heterocycloalkyl, aryl, heteroaryl,  
 20 aralkyl, heteroaralkyl, aralkoxy, heteroaralkoxy,  
 aralkoxyalkyl, aryloxyalkyl, aralkanoylalkyl,  
 arylcarbonylalkyl, aralkylaryl, aryloxyalkylaryl,  
 aralkoxyaryl, arylazoaryl, arylhydrazinoaryl,  
 alkylthioaryl, arylthioalkyl, alkylthioaralkyl,  
 25 aralkylthioalkyl, an aralkylthioaryl radical, the  
 sulfoxide or sulfone of any of the thio substituents,  
 and a fused ring structure comprising two or more 5-

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or 6-membered rings selected from the group consisting of aryl, heteroaryl, cycloalkyl and heterocycloalkyl, and (b) is itself optionally substituted with one or more substituents

5 independently selected from the group consisting of a cyano, perfluoroalkyl, trifluoromethoxy, trifluoromethylthio, haloalkyl, trifluoromethylalkyl, aralkoxycarbonyl, aryloxycarbonyl, hydroxy, halo, alkyl, alkoxy, nitro, thiol, hydroxycarbonyl,

10 aryloxy, arylthio, aralkyl, aryl, arylcarbonylamino, heteroaryloxy, heteroarylthio, heteroaralkyl, cycloalkyl, heterocyclooxy, heterocyclothio, heterocycloamino, cycloalkyloxy, cycloalkylthio, heteroaralkoxy, heteroaralkylthio, aralkoxy,

15 aralkylthio, aralkylamino, heterocyclo, heteroaryl, arylazo, hydroxycarbonylalkoxy, alkoxycarbonylalkoxy, alkanoyl, arylcarbonyl, aralkanoyl, alkanoyloxy, aralkanoyloxy, hydroxyalkyl, hydroxyalkoxy, alkylthio, alkoxyalkylthio, alkoxycarbonyl,

20 aryloxyalkoxyaryl, arylthioalkylthioaryl, aryloxyalkylthioaryl, arylthioalkoxyaryl, hydroxycarbonylalkoxy, hydroxycarbonylalkylthio, alkoxycarbonylalkoxy, alkoxycarbonylalkylthio, amino,

25 wherein the amino nitrogen is (i) unsubstituted, or (ii) substituted with one or two substituents that are independently selected from the group consisting of an alkyl, aryl, heteroaryl, aralkyl, cycloalkyl, aralkoxycarbonyl, alkoxycarbonyl, arylcarbonyl, aralkanoyl, heteroarylcarbonyl, heteroaralkanoyl and an

30 alkanoyl group, or (iii) wherein the amino nitrogen and two substituents attached thereto form a 5- to 8-membered heterocyclo or



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hydroxy, hydroxycarbonyl, aryl, aralkyl,  
heteroaralkyl and an amino group,

wherein the amino nitrogen is

(i) unsubstituted, or (ii) substituted with  
one or two substituents that are  
independently selected from the group  
consisting of alkyl, aryl, and heteroaryl,  
or (iii) wherein the amino nitrogen and two  
substituents attached thereto form a 5- to  
8-membered heterocyclo or heteroaryl ring,

and an aminoalkyl group

wherein the aminoalkyl nitrogen is (i)  
unsubstituted, or (ii) substituted with one or two  
substituents independently selected from the group  
consisting of an alkyl, aryl, aralkyl, cycloalkyl,  
aralkoxycarbonyl, alkoxycarbonyl, and an alkanoyl  
group, or (iii) wherein the aminoalkyl nitrogen and  
two substituents attached thereto form a 5- to 8-  
membered heterocyclo or heteroaryl ring; and

Z is selected group the group consisting of  
O, S,  $\text{NR}^6$ , SO,  $\text{SO}_2$ , and  $\text{NSO}_2\text{R}^7$ ,

wherein  $\text{R}^6$  is selected from the group  
consisting of hydrido,  $\text{C}_1\text{-C}_5\text{-alkyl}$ ,  $\text{C}_1\text{-C}_5\text{-alkanoyl}$ ,  
benzyl, benzoyl,  $\text{C}_3\text{-C}_5\text{-alkynyl}$ ,  $\text{C}_3\text{-C}_5\text{-alkenyl}$ ,  $\text{C}_1\text{-C}_3\text{-}$   
 $\text{alkoxy-C}_1\text{-C}_4\text{-alkyl}$ ,  $\text{C}_3\text{-C}_6\text{-cycloalkyl}$ , heteroaryl- $\text{C}_1\text{-}$   
 $\text{C}_6\text{-alkyl}$ ,  $\text{C}_1\text{-C}_5\text{-hydroxyalkyl}$ ,  $\text{C}_1\text{-C}_5\text{-carboxyalkyl}$ ,  $\text{C}_1\text{-}$   
 $\text{C}_5\text{-alkoxy C}_1\text{-C}_5\text{-alkylcarbonyl}$ , and  $\text{NR}^8\text{R}^9\text{-C}_1\text{-C}_5\text{-}$   
 $\text{alkylcarbonyl}$  or  $\text{NR}^8\text{R}^9\text{-C}_1\text{-C}_5\text{-alkyl}$  wherein  $\text{R}^8$  and  $\text{R}^9$   
are independently hydrido,  $\text{C}_1\text{-C}_5\text{-alkyl}$ ,  $\text{C}_1\text{-C}_5\text{-}$

alkoxycarbonyl or aryl-C<sub>1</sub>-C<sub>5</sub>-alkoxycarbonyl, or NR<sup>8</sup>R<sup>9</sup> together form a heterocyclic ring containing 5- to 8-atoms in the ring; and

R<sup>7</sup> is selected from the group consisting of a arylalkyl, aryl, heteroaryl, heterocyclo, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub>-alkynyl, C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>1</sub>-C<sub>6</sub>-carboxyalkyl and a C<sub>1</sub>-C<sub>6</sub>-hydroxyalkyl group.

21. The process according to claim 20 wherein R<sup>3</sup> is a single-ringed aryl or heteroaryl group that is 5- or 6-membered, and is itself substituted at its own 4-position when a 6-membered ring or at its own 3- or 4-position when a 5-membered ring with a substituent selected from the group consisting of one other single-ringed aryl or heteroaryl group, a C<sub>3</sub>-C<sub>14</sub> alkyl group, a N-piperidyl group, a N-piperazinyl group, a phenoxy group, a thiophenoxy group, a 4-thiopyridyl group, a phenylazo group and a benzamido group.

22. The process according to claim 20 wherein R<sup>3</sup> has a length that is greater than that of a pentyl group and a length that is less than that of an icosyl group.

~~23. The process according to claim 20 wherein Z is O, S or NR<sup>6</sup>.~~

24. The process according to claim 23 wherein R<sup>6</sup> is selected from the group consisting of

C<sub>3</sub>-C<sub>6</sub>-cycloalkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>3</sub>-C<sub>6</sub>-alkynyl, amino-C<sub>1</sub>-C<sub>6</sub>-alkyl, aminosulfonyl, heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxycarbonyl, and C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonyl.

5

25. The process according to claim 20 wherein said R<sup>3</sup> radical is the substituent G-A-R-E-Y, wherein G is an aryl or heteroaryl group;

A is selected from the group consisting of

10

(1) -O-;

(2) -S-;

(3) -NR<sup>17</sup>-;

(4) -CO-N(R<sup>17</sup>) or -N(R<sup>17</sup>)-CO-, wherein R<sup>17</sup> is hydrogen, C<sub>1</sub>-C<sub>4</sub>-alkyl, or phenyl;

15

(5) -CO-O- or -O-CO-;

(6) -O-CO-O-;

(7) -HC=CH-;

(8) -NH-CO-NH-;

(9) -C≡C-;

20

(10) -NH-CO-O- or -O-CO-NH-;

(11) -N=N-;

(12) -NH-NH-; and

(13) -CS-N(R<sup>18</sup>)- or -N(R<sup>18</sup>)-CS-, wherein R<sup>18</sup> is hydrogen C<sub>1</sub>-C<sub>4</sub>-alkyl, or

25

phenyl; or

(14) A is absent and G is bonded directly to R;

R is a moiety selected from the group consisting of alkyl, alkoxyalkyl, aryl, heteroaryl,

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cycloalkyl, heterocycloalkyl, aralkyl, heteroaralkyl,  
heterocycloalkylalkyl, cycloalkylalkyl,  
cycloalkoxyalkyl, heterocycloalkoxyalkyl,  
aryloxyalkyl, heteroaryloxyalkyl, arylthioalkyl,  
5 heteroarylthioalkyl, cycloalkylthioalkyl, and a  
heterocycloalkylthioalkyl group wherein the aryl or  
heteroaryl or cycloalkyl or heterocycloalkyl  
substituent is (i) unsubstituted or (ii) substituted  
with one or two radicals selected from the group  
10 consisting of a halo, alkyl, perfluoroalkyl,  
perfluoroalkoxy, perfluoroalkylthio,  
trifluoromethylalkyl, amino, alkoxycarbonylalkyl,  
alkoxy, C<sub>1</sub>-C<sub>2</sub>-alkylene-dioxy, hydroxycarbonylalkyl,  
hydroxycarbonylalkylamino, nitro, hydroxy,  
15 hydroxyalkyl, alkanoylamino, and a alkoxycarbonyl  
group, and R is other than alkyl or alkoxyalkyl when  
A is -O- or -S-;

E is selected from the group consisting of

- (1) -CO(R<sup>19</sup>)- or -(R<sup>19</sup>)CO-, wherein R<sup>19</sup> is  
20 a heterocycloalkyl, or a cycloalkyl  
group;  
(2) -CONH- or -HNCO-; and  
(3) -CO-;  
(4) -SO<sub>2</sub>-R<sup>19</sup>- or -R<sup>19</sup>-SO<sub>2</sub>-;  
25 (5) -SO<sub>2</sub>-;  
(6) -NH-SO<sub>2</sub>- or -SO<sub>2</sub>-NH-; or  
(7) E is absent and R is bonded directly  
to Y; and

Y is absent or is selected from the group  
30 consisting of a hydrido, alkyl, alkoxy, haloalkyl,

aryl, aralkyl, cycloalkyl, heteroaryl, hydroxy,  
aryloxy, aralkoxy, heteroaryloxy, heteroaralkyl,  
perfluoroalkoxy, perfluoroalkylthio,  
trifluoromethylalkyl, alkenyl, heterocycloalkyl,  
5 cycloalkyl, trifluoromethyl, alkoxycarbonyl, and a  
aminoalkyl group, wherein the aryl or heteroaryl or  
heterocycloalkyl group is (i) unsubstituted or (ii)  
substituted with one or two radicals independently  
selected from the group consisting of an alkanoyl,  
10 halo, nitro, aralkyl, aryl, alkoxy, and an amino  
group wherein the amino nitrogen is (i) unsubstituted  
or (ii) substituted with one or two groups  
independently selected from hydrido, alkyl, and an  
aralkyl group.

15

*Set p10*  
~~26. The process according to claim 25~~  
wherein said -G-A-R-E-Y substituent contains two to  
four carbocyclic or heterocyclic rings.

20

27. The process according to claim 26  
wherein each of the two to four rings is 6-membered.

28. The process according to claim 25  
wherein said -G-A-R-E-Y substituent has a length that  
25 is greater than a hexyl group and a length that is  
~~less than that of a stearyl group.~~

30

29. The process according to claim 25  
wherein A is -O- or -S-

30. The process according to claim 25 wherein R is an aryl, heteroaryl, cycloalkyl or heterocycloalkyl group.

5 31. The process according to claim 25 wherein E is absent.

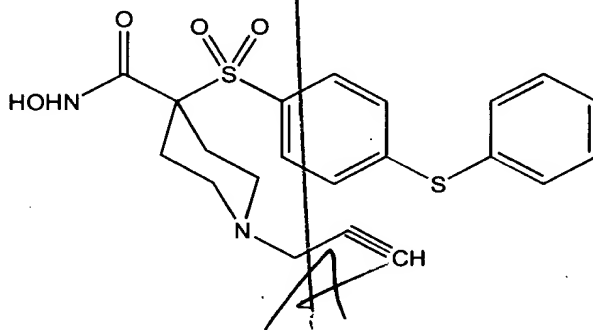
32. The process according to claim 25 wherein Y is selected from the group consisting of  
10 hydrido, an alkyl, alkoxy, perfluoroalkoxy and a perfluoroalkylthio group.

33. The process according to claim 20 wherein R<sup>3</sup> is a radical that is comprised of a  
15 single-ringed aryl or heteroaryl group that is 5- or 6-membered, and is itself substituted at its own 4-position when a 6-membered ring and at its own 3- or 4-position when a 5-membered ring with a substituent selected from the group consisting of a thiophenoxy,  
20 4-chlorophenoxy, 3-chlorophenoxy, 4-methoxyphenoxy, 3-benzodioxol-5-yloxy, 3,4-dimethylphenoxy, 4-fluorophenoxy, 4-fluorothiophenoxy, phenoxy, 4-trifluoromethoxy-phenoxy, 4-trifluoromethylphenoxy, 4-(trifluoromethylthio)-phenoxy, 4-  
25 (trifluoromethylthio)-thiophenoxy, 4-chloro-3-fluorophenoxy, 4-isopropoxyphenoxy, 4-isopropylphenoxy, (2-methyl-1,3-benzothiazol-5-yl)oxy, 4-(1H-imidazol-1-yl)phenoxy, 4-chloro-3-methylphenoxy, 3-methylphenoxy, 4-ethoxyphenoxy, 3,4-  
30 difluorophenoxy, 4-chloro-3-methylphenoxy, 4-fluoro-3-chlorophenoxy, 4-(1H-1,2,4-triazol-1-yl)phenoxy, 3,5-difluorophenoxy, 3,4-dichlorophenoxy, 4-

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cyclopentylphenoxy, 4-bromo-3-methylphenoxy, 4-bromophenoxy, 4-methylthiophenoxy, 4-phenylphenoxy, 4-benzylphenoxy, 6-quinolinyloxy, 4-amino-3-methylphenoxy, 3-methoxyphenoxy, 5,6,7,8-tetrahydro-  
5 2-naphthalenyloxy, 3-hydroxymethylphenoxy, N-piperidyl, N-piperazinyl and a 4-benzyloxyphenoxy group.

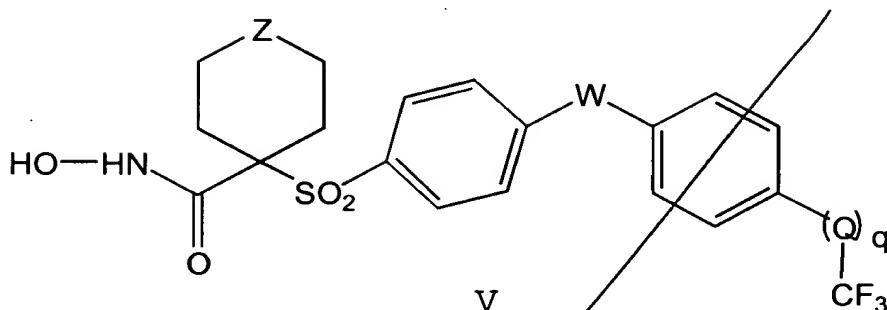
34. The process according to claim 20  
10 wherein said inhibitor corresponds in structure to the formula



35. A process for treating a host mammal  
15 having a condition associated with pathological matrix metalloprotease (MMP) activity that comprises administering a metalloprotease inhibitor compound or a pharmaceutically acceptable salt thereof in an effective amount to a mammalian host having such a  
20 condition, said metalloprotease inhibitor inhibiting the activity of one or more of MMP-2, MMP-9 and MMP-13, while exhibiting substantially less inhibitory activity against MMP-1, said compound corresponding in structure to formula V, below

25





wherein

Z is O, S or NR<sup>6</sup>;

5           W and Q are independently oxygen (O), NR<sup>6</sup>  
or sulfur (S),

          R<sup>6</sup> is selected from the group consisting of  
C<sub>3</sub>-C<sub>6</sub>-cycloalkyl, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>3</sub>-C<sub>6</sub>-  
alkynyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, amino-C<sub>1</sub>-C<sub>6</sub>-alkyl,  
10   aminosulfonyl, heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkyl,  
aryloxycarbonyl, and C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonyl; and

          q is zero or one such that when q is zero,  
Q is absent and the trifluoromethyl group is bonded  
directly to the depicted phenyl ring.

15

36. The process according to claim 35  
wherein q is zero.

37. The process according to claim 35  
20   wherein W is O.

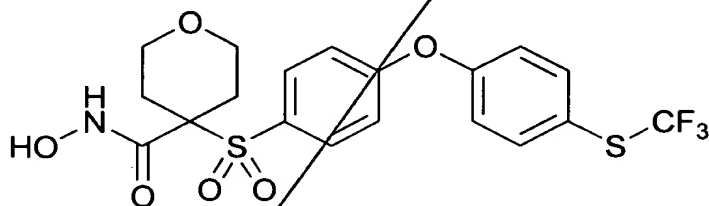
38. The process according to claim 37  
wherein q is zero.

39. The process according to claim 37  
25   wherein q is one and Q is O.

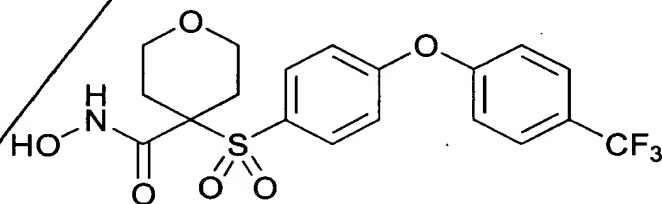
604450-1-2-3-4-5-6-7-8-9-10-11-12-13-14-15-16-17-18-19-20-21-22-23-24-25-26-27-28-29-30-31-32-33-34-35-36-37-38-39-40-41-42-43-44-45-46-47-48-49-50-51-52-53-54-55-56-57-58-59-60

40. The process according to claim 37 wherein q is one and Q is S.

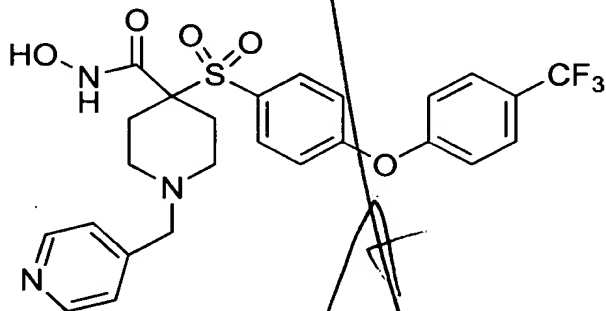
*B12* 5 ~~41. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula~~



10 42. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula

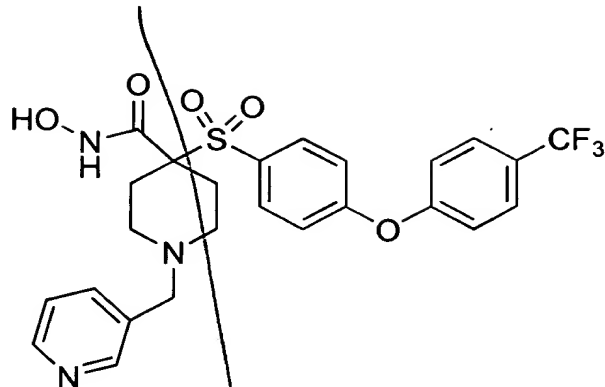


15 43. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula

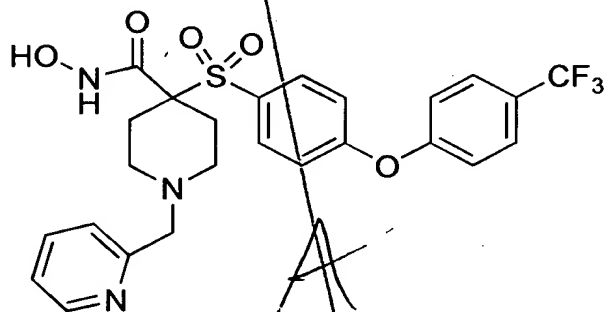


44. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula

667730 4637660

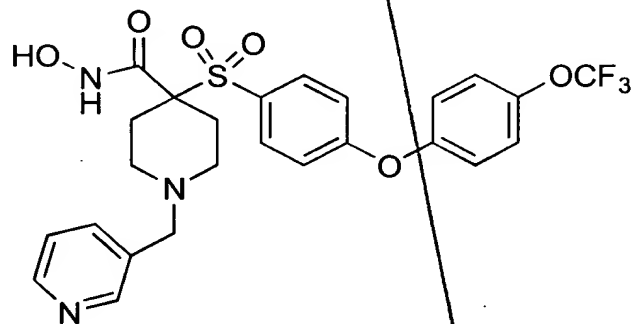


45. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula



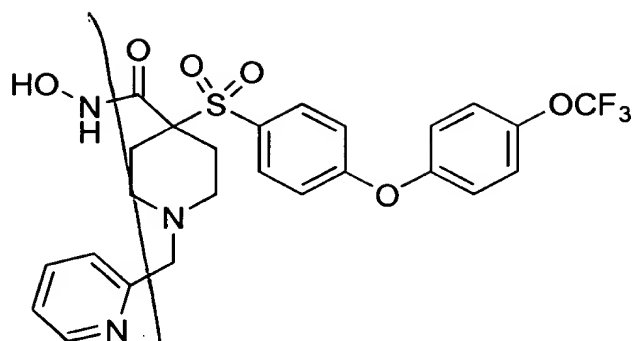
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46. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula

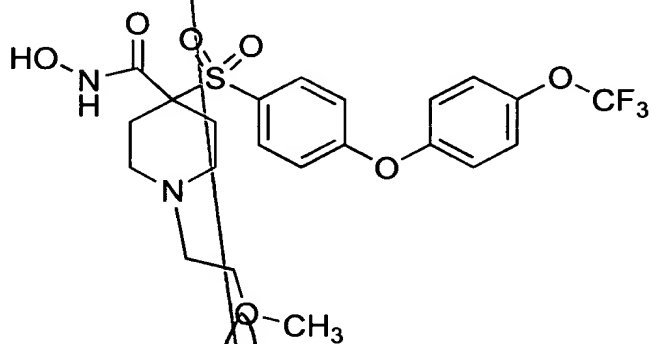


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47. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula

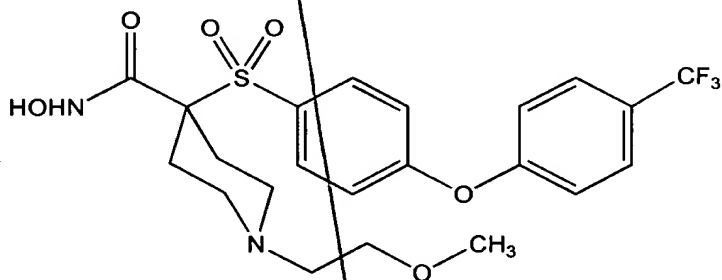


48. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula



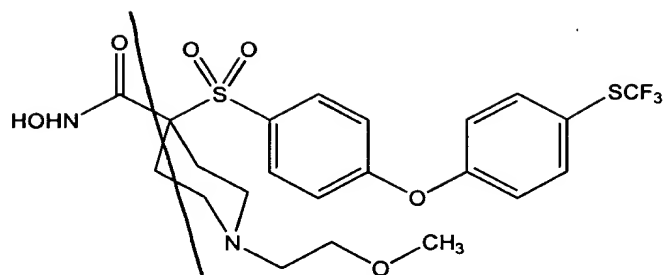
5

49. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula

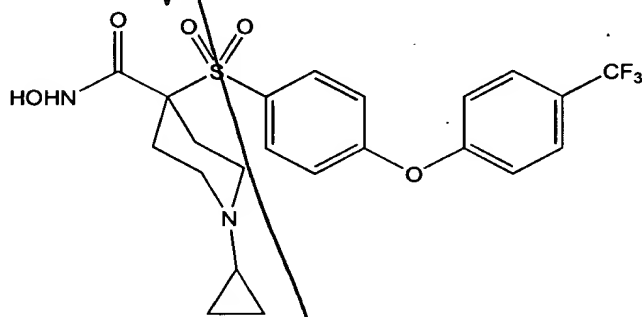


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50. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula

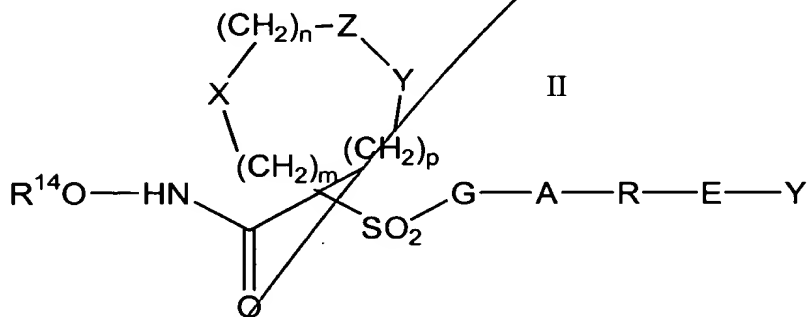


51. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula



5

52. A compound corresponding in structure to formula II, below, or a pharmaceutically acceptable salt thereof:



10

wherein

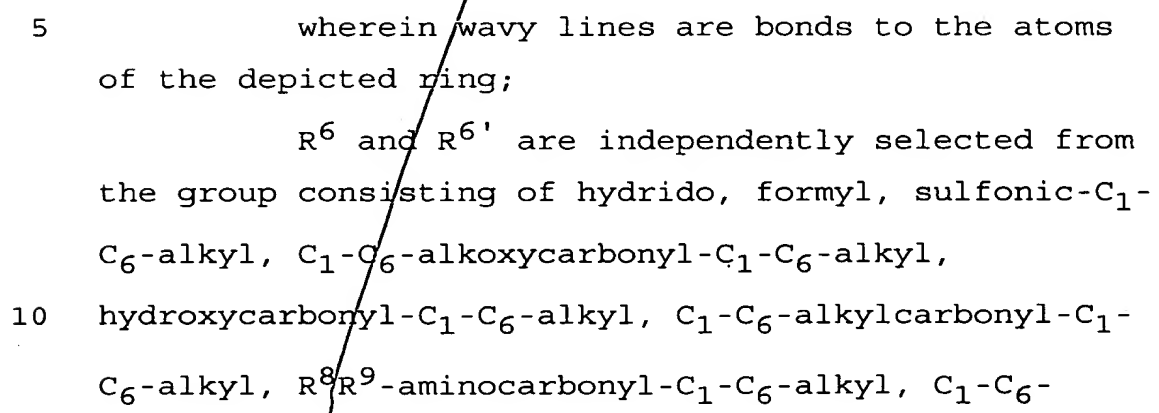
$\text{R}^{14}$  is hydrido, a pharmaceutically acceptable cation or  $\text{C(W)}\text{R}^{15}$  where W is O or S and  $\text{R}^{15}$  is selected from the group consisting of an  $\text{C}_1$ - $\text{C}_6$ -alkyl, aryl,  $\text{C}_1$ - $\text{C}_6$ -alkoxy, heteroaryl- $\text{C}_1$ - $\text{C}_6$ -alkyl,

C<sub>3</sub>-C<sub>8</sub>-cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy, ar-C<sub>1</sub>-C<sub>6</sub>-alkoxy, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryl and amino C<sub>1</sub>-C<sub>6</sub>-alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two substituents independently selected from the group consisting of an C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>3</sub>-C<sub>8</sub>-cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, ar-C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonyl, and C<sub>1</sub>-C<sub>6</sub>-alkanoyl radical, or (iii) wherein the amino C<sub>1</sub>-C<sub>6</sub>-alkyl nitrogen and two substituents attached thereto form a 5- to 8-membered heterocyclo or heteroaryl ring;

m is zero, 1 or 2;  
n is zero, 1 or 2;  
p is zero, 1 or 2;  
the sum of m + n + p = 1, 2, 3 or 4;  
(a) one of X, Y and Z is selected from the group consisting of C(O), NR<sup>6</sup>, O, S, S(O), S(O)<sub>2</sub> and NS(O)<sub>2</sub>R<sup>7</sup>, and the remaining two of X, Y and Z are CR<sup>8</sup>R<sup>9</sup>, and CR<sup>10</sup>R<sup>11</sup>, or

(b) X and Z or Z and Y together constitute a moiety that is selected from the group consisting of NR<sup>6</sup>C(O), NR<sup>6</sup>S(O), NR<sup>6</sup>S(O)<sub>2</sub>, NR<sup>6</sup>S, NR<sup>6</sup>O, SS, NR<sup>6</sup>NR<sup>6</sup> and OC(O), with the remaining one of X, Y and Z being CR<sup>8</sup>R<sup>9</sup>, or

(c) n is zero and X, Y and Z together constitute a moiety selected from the group consisting of



10

- alkoxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl, hydroxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonylcarbonyl, hydroxycarbonylcarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkylcarbonylcarbonyl,
- 5 R<sup>8</sup>R<sup>9</sup>-aminocarbonylcarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkanoyl, aryl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aroyl, bis(C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl)-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-haloalkyl, C<sub>1</sub>-C<sub>6</sub>-perfluoroalkyl, C<sub>1</sub>-C<sub>6</sub>-trifluoromethylalkyl, C<sub>1</sub>-C<sub>6</sub>-perfluoroalkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-
- 10 alkyl, C<sub>3</sub>-C<sub>6</sub>-cycloalkyl, heteroarycarbonyl, heterocyclocarbonyl, C<sub>3</sub>-C<sub>8</sub>-heterocycloalkyl, C<sub>3</sub>-C<sub>8</sub>-heterocycloalkylcarbonyl, aryl, C<sub>5</sub>-C<sub>6</sub>-heterocyclo, C<sub>5</sub>-C<sub>6</sub>-heteroaryl, C<sub>3</sub>-C<sub>8</sub>-cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl,
- 15 heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroarylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, arylsulfonyl, C<sub>1</sub>-C<sub>6</sub>-alkylsulfonyl, C<sub>5</sub>-C<sub>6</sub>-heteroarylsulfonyl, carboxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>4</sub>-alkoxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aminocarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkyl(R<sup>8</sup>N)iminocarbonyl, aryl(R<sup>8</sup>N)iminocarbonyl, C<sub>5</sub>-
- 20 C<sub>6</sub>-heterocyclo(R<sup>8</sup>N)iminocarbonyl, arylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, arylthio-C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>1</sub>-C<sub>4</sub>-alkylthio-C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>5</sub>-C<sub>6</sub>-heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkyl, halo-C<sub>1</sub>-C<sub>6</sub>-alkanoyl, hydroxy-C<sub>1</sub>-C<sub>6</sub>-alkanoyl, thiol-C<sub>1</sub>-C<sub>6</sub>-alkanoyl, C<sub>3</sub>-C<sub>6</sub>-alkenyl,
- 25 C<sub>3</sub>-C<sub>6</sub>-alkynyl, C<sub>1</sub>-C<sub>4</sub>-alkoxy-C<sub>1</sub>-C<sub>4</sub>-alkyl, C<sub>1</sub>-C<sub>5</sub>-alkoxycarbonyl, aryloxycarbonyl, NR<sup>8</sup>R<sup>9</sup>-(R<sup>8</sup>)iminomethyl, NR<sup>8</sup>R<sup>9</sup>-C<sub>1</sub>-C<sub>5</sub>-alkylcarbonyl, hydroxy-



C<sub>1</sub>-C<sub>5</sub>-alkyl, R<sup>8</sup>R<sup>9</sup>-aminocarbonyl, R<sup>8</sup>R<sup>9</sup>-aminocarbonyl-  
C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl, hydroxyaminocarbonyl, R<sup>8</sup>R<sup>9</sup>-  
aminosulfonyl, R<sup>8</sup>R<sup>9</sup>-aminosulfon-C<sub>1</sub>-C<sub>6</sub>-alkyl, R<sup>8</sup>R<sup>9</sup>-  
amino-C<sub>1</sub>-C<sub>6</sub>-alkylsulfonyl and an R<sup>8</sup>R<sup>9</sup>-amino-C<sub>1</sub>-C<sub>6</sub>-  
5 alkyl group;

R<sup>7</sup> is selected from the group consisting of  
a arylalkyl, aryl, heteroaryl, heterocyclo, C<sub>1</sub>-C<sub>6</sub>-  
alkyl, C<sub>3</sub>-C<sub>6</sub>-alkynyl, C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>1</sub>-C<sub>6</sub>-  
carboxyalkyl and a C<sub>1</sub>-C<sub>6</sub>-hydroxyalkyl group;

10 R<sup>8</sup> and R<sup>9</sup> and R<sup>10</sup> and R<sup>11</sup> are independently  
selected from the group consisting of a hydrido,  
hydroxy, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkanoyl, aroyl, aryl,  
ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryl, heteroar-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>2</sub>-  
C<sub>6</sub>-alkynyl, C<sub>2</sub>-C<sub>6</sub>-alkenyl, thiol-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-  
15 alkylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, cycloalkyl, cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-  
alkyl, heterocycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-  
C<sub>6</sub>-alkyl, aralkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-  
alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxy-C<sub>1</sub>-C<sub>6</sub>-alkyl,  
hydroxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxycarbonylar-C<sub>1</sub>-C<sub>6</sub>-  
20 alkyl, aminocarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-  
alkyl, heteroaryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, arylthio-C<sub>1</sub>-C<sub>6</sub>-  
alkyl, heteroarylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, the sulfoxide or  
sulfone of any said thio substituents, perfluoro-C<sub>1</sub>-  
C<sub>6</sub>-alkyl, trifluoromethyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, halo-C<sub>1</sub>-C<sub>6</sub>-  
25 alkyl, alkoxycarbonylamino-C<sub>1</sub>-C<sub>6</sub>-alkyl and an amino-  
C<sub>1</sub>-C<sub>6</sub>-alkyl group wherein the aminoalkyl nitrogen is  
(i) unsubstituted or (ii) substituted with one or two

radicals independently selected from the group consisting of C<sub>1</sub>-C<sub>6</sub>-alkyl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, cycloalkyl and C<sub>1</sub>-C<sub>6</sub>-alkanoyl, or wherein R<sup>8</sup> and R<sup>9</sup> or R<sup>10</sup> and R<sup>11</sup> and the carbon to which they are bonded form a carbonyl group, or wherein R<sup>8</sup> and R<sup>9</sup> or R<sup>10</sup> and R<sup>11</sup>, or R<sup>8</sup> and R<sup>10</sup> together with the atoms to which they are bonded form a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclic or heteroaryl ring containing one or two heteroatoms that are nitrogen, oxygen, or sulfur, with the proviso that only one of R<sup>8</sup> and R<sup>9</sup> or R<sup>10</sup> and R<sup>11</sup> is hydroxy;

R<sup>12</sup> and R<sup>12'</sup> are independently selected from the group consisting of a hydrido, C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryl, heteroaralkyl, C<sub>2</sub>-C<sub>6</sub>-alkynyl, C<sub>2</sub>-C<sub>6</sub>-alkenyl, thiol-C<sub>1</sub>-C<sub>6</sub>-alkyl, cycloalkyl, cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, heterocycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, amino-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxycarbonylar-C<sub>1</sub>-C<sub>6</sub>-alkyl, aminocarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, arylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroarylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, the sulfoxide or sulfone of any said thio substituents, perfluoro-C<sub>1</sub>-C<sub>6</sub>-alkyl, trifluoromethyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, halo-C<sub>1</sub>-C<sub>6</sub>-alkyl, alkoxycarbonylamino-C<sub>1</sub>-C<sub>6</sub>-alkyl and an amino-C<sub>1</sub>-C<sub>6</sub>-alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii)

substituted with one or two radicals independently selected from the group consisting of  $C_1-C_6$ -alkyl, ar- $C_1-C_6$ -alkyl, cycloalkyl and  $C_1-C_6$ -alkanoyl;

$R^{13}$  is selected from the group consisting of a hydrido, benzyl, phenyl,  $C_1-C_6$ -alkyl,  $C_2-C_6$ -alkynyl,  $C_2-C_6$ -alkenyl and a  $C_1-C_6$ -hydroxyalkyl group; and

G-A-R-E-Y is a substituent that has a length greater than that of a pentyl group a length that is less than that of an icosyl group, and wherein

G is an aryl or heteroaryl group;

A is selected from the group consisting of

- (1) -O-;
- (2) -S-;
- (3) -NR<sup>17</sup>-;
- (4) -CO-N(R<sup>17</sup>) or -N(R<sup>17</sup>)-CO-, wherein R<sup>17</sup> is hydrogen,  $C_1-C_4$ -alkyl, or phenyl;
- (5) -CO-O- or -O-CO-;
- (6) -O-CO-O-;
- (7) -HC=CH-;
- (8) -NH-CO-NH-;
- (9) -C≡C-;
- (10) -NH-CO-O- or -O-CO-NH-;
- (11) -N=N-;
- (12) -NH-NH-; and
- (13) -CS-N(R<sup>18</sup>)- or -N(R<sup>18</sup>)-CS-, wherein R<sup>18</sup> is hydrogen  $C_1-C_4$ -alkyl, or phenyl; or

(14) A is absent and G is bonded directly to R;

R is a moiety selected from the group consisting of alkyl, alkoxyalkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, aralkyl, heteroaralkyl, heterocycloalkylalkyl, cycloalkylalkyl, cycloalkoxyalkyl, heterocycloalkoxyalkyl, aryloxyalkyl, heteroaryloxyalkyl, arylthioalkyl, heteroarylthioalkyl, cycloalkylthioalkyl, and a heterocycloalkylthioalkyl group wherein the aryl or heteroaryl or cycloalkyl or heterocycloalkyl substituent is (i) unsubstituted or (ii) substituted with one or two radicals selected from the group consisting of a halo, alkyl, perfluoroalkyl, perfluoroalkoxy, perfluoroalkylthio, trifluoromethylalkyl, amino, alkoxycarbonylalkyl, alkoxy, C<sub>1</sub>-C<sub>2</sub>-alkylene-dioxy, hydroxycarbonylalkyl, hydroxycarbonylalkylamino, nitro, hydroxy, hydroxyalkyl, alkanoylamino, and a alkoxycarbonyl group, and R is other than alkyl or alkoxyalkyl when A is -O- or -S-;

E is selected from the group consisting of

- (1) -CO(R<sup>19</sup>)- or -(R<sup>19</sup>)CO-, wherein R<sup>19</sup> is a heterocycloalkyl, or a cycloalkyl group;
- (2) -CONH- or -HNCO-; and
- (3) -CO-;
- (4) -SO<sub>2</sub>-R<sup>19</sup>- or -R<sup>19</sup>-SO<sub>2</sub>-;
- (5) -SO<sub>2</sub>-;
- (6) -NH-SO<sub>2</sub>- or -SO<sub>2</sub>-NH-; or

(7) E is absent and R is bonded directly to Y; and

Y is absent or is selected from the group consisting of a hydrido, alkyl, alkoxy, haloalkyl, aryl, aralkyl, cycloalkyl, heteroaryl, hydroxy, aryloxy, aralkoxy, heteroaryloxy, heteroaralkyl, perfluoroalkoxy, perfluoroalkylthio, trifluoromethylalkyl, alkenyl, heterocycloalkyl, cycloalkyl, trifluoromethyl, alkoxycarbonyl, and a aminoalkyl group, wherein the aryl or heteroaryl or heterocycloalkyl group is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of an alkanoyl, halo, nitro, aralkyl, aryl, alkoxy, and an amino group wherein the amino nitrogen is (i) unsubstituted or (ii) substituted with one or two groups independently selected from hydrido, alkyl, and an aralkyl group.

53. The compound or salt according to claim 52 wherein said -G-A-R-E-Y substituent contains two to four carbocyclic or heterocyclic rings.

54. The compound or salt according to claim 52 wherein each of the two to four rings is 6-membered.

55. The compound or salt according to claim 52 wherein said -G-A-R-E-Y substituent has a length that is greater than a hexyl group and a length that is less than that of a stearyl group.

56. The compound or salt according to claim 52 wherein A is -O- or -S-.

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5 ~~57. The compound or salt according to claim 52 wherein R is an aryl, heteroaryl, cycloalkyl or heterocycloalkyl group.~~

10 58. The compound or salt according to claim 52 wherein E is absent.

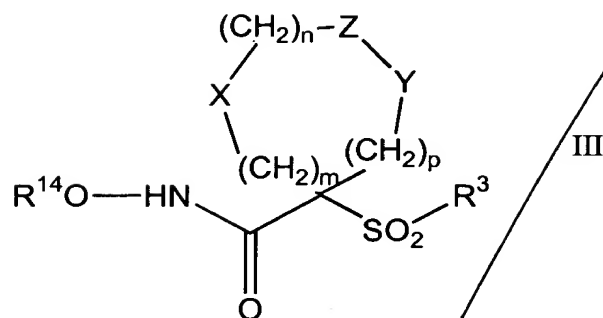
15 59. The compound or salt according to claim 52 wherein Y is selected from the group consisting of hydrido, an alkyl, alkoxy, perfluoroalkoxy and a perfluoroalkylthio group.

60. The compound or salt according to claim 52 wherein  $R^{14}$  is hydrido.

20 61. The compound or salt according to claim 52 wherein W of the  $C(W)R^{15}$  is O and  $R^{15}$  is a  $C_1$ - $C_6$ -alkyl, aryl,  $C_1$ - $C_6$ -alkoxy, heteroaryl- $C_1$ - $C_6$ -alkyl,  $C_3$ - $C_8$ -cycloalkyl- $C_1$ - $C_6$ -alkyl, or aryloxy group.

25 62. A compound corresponding in structure to formula III, below, or a pharmaceutically acceptable salt thereof

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wherein

$R^3$  is a single-ringed aryl or heteroaryl group that is 5- or 6-membered, and is itself substituted at its own 4-position when a 6-membered ring and at its own 3- or 4-position when a 5-membered ring with a substituent selected from the group consisting of a thiophenoxy, 4-chloro-phenoxy, 3-chlorophenoxy, 4-methoxyphenoxy, 3-benzodioxol-5-yloxy, 3,4-dimethylphenoxy, 4-fluorophenoxy, 4-fluorothiophenoxy, phenoxy, 4-trifluoromethoxyphenoxy, 4-trifluoromethylphenoxy, 4-(trifluoromethylthio)phenoxy, 4-(trifluoromethylthio)thiophenoxy, 4-chloro-3-fluorophenoxy, 4-isopropoxyphenoxy, 4-isopropylphenoxy, (2-methyl-1,3-benzothiazol-5-yl)oxy, 4-(1H-imidazol-1-yl)phenoxy, 4-chloro-3-methylphenoxy, 3-methyl-phenoxy, 4-ethoxyphenoxy, 3,4-difluorophenoxy, 4-chloro-3-methylphenoxy, 4-fluoro-3-chlorophenoxy, 4-(1H-1,2,4-triazol-1-yl)phenoxy, 3,5-difluorophenoxy, 3,4-dichlorophenoxy, 4-cyclopentylphenoxy, 4-bromo-3-methylphenoxy, 4-bromophenoxy, 4-methylthiophenoxy, 4-phenylphenoxy, 4-benzylphenoxy, 6-quinolinyloxy, 4-amino-3-methylphenoxy, 3-methoxyphenoxy, 5,6,7,8-tetrahydro-2-naphthalenyloxy, 3-hydroxymethylphenoxy, and a 4-benzyloxyphenoxy group;

5  $R^{14}$  is hydrido, a pharmaceutically acceptable cation or  $C(W)R^{15}$  where W is O or S and  $R^{15}$  is selected from the group consisting of a  $C_1-C_6$ -alkyl, aryl,  $C_1-C_6$ -alkoxy, heteroaryl- $C_1-C_6$ -alkyl,  $C_3-C_8$ -cycloalkyl- $C_1-C_6$ -alkyl, aryloxy, ar- $C_1-C_6$ -alkoxy, ar- $C_1-C_6$ -alkyl, heteroaryl and amino  $C_1-C_6$ -alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two substituents independently selected from the group consisting of an  $C_1-C_6$ -alkyl, aryl, ar- $C_1-C_6$ -alkyl,  $C_3-C_8$ -cycloalkyl- $C_1-C_6$ -alkyl, ar- $C_1-C_6$ -alkoxycarbonyl,  $C_1-C_6$ -alkoxycarbonyl, and  $C_1-C_6$ -alkanoyl radical, or (iii) wherein the amino  $C_1-C_6$ -alkyl nitrogen and two substituents attached thereto form a 5- to 8-membered heterocyclo or heteroaryl ring;

m is zero, 1 or 2;

n is zero, 1 or 2;

p is zero, 1 or 2;

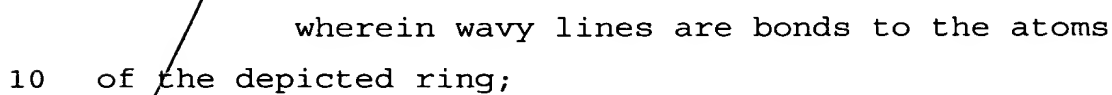
20 the sum of  $m + n + p = 1, 2, 3$  or 4;

(a) one of X, Y and Z is selected from the group consisting of  $C(O)$ ,  $NR^6$ , O, S,  $S(O)$ ,  $S(O)_2$  and  $NS(O)_2R^7$ , and the remaining two of X, Y and Z are  $CR^8R^9$ , and  $CR^{10}R^{11}$ , or

25 (b) X and Z or Z and Y together constitute a moiety that is selected from the group consisting of  $NR^6C(O)$ ,  $NR^6S(O)$ ,  $NR^6S(O)_2$ ,  $NR^6S$ ,  $NR^6O$ ,  $SS$ ,  $NR^6NR^6$  and  $OC(O)$ , with the remaining one of X, Y and Z being  $CR^8R^9$ , or



5



$R^6$  and  $R^{6'}$  are independently selected from the group consisting of hydrido, formyl, sulfonic- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkoxycarbonyl- $C_1$ - $C_6$ -alkyl, hydroxycarbonyl- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkylcarbonyl- $C_1$ - $C_6$ -alkyl,  $R^8R^9$ -aminocarbonyl- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkoxycarbonyl- $C_1$ - $C_6$ -alkylcarbonyl, hydroxycarbonyl- $C_1$ - $C_6$ -alkylcarbonyl,  $C_1$ - $C_6$ -alkylcarbonyl- $C_1$ - $C_6$ -alkylcarbonyl,  $C_1$ - $C_6$ -alkoxycarbonylcarbonyl, hydroxycarbonylcarbonyl,  $C_1$ - $C_6$ -alkylcarbonylcarbonyl,  $R^8R^9$ -aminocarbonylcarbonyl,  $C_1$ - $C_6$ -alkanoyl, aryl- $C_1$ - $C_6$ -alkyl, aroyl, bis( $C_1$ - $C_6$ -alkoxy- $C_1$ - $C_6$ -alkyl)- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -haloalkyl,  $C_1$ - $C_6$ -perfluoroalkyl,  $C_1$ - $C_6$ -trifluoromethylalkyl,  $C_1$ - $C_6$ -perfluoroalkoxy- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkoxy- $C_1$ - $C_6$ -alkyl,  $C_3$ - $C_6$ -cycloalkyl, heteroarycarbonyl, heterocyclocarbonyl,  $C_3$ - $C_8$ -heterocycloalkyl,  $C_3$ - $C_8$ -heterocycloalkylcarbonyl, aryl,  $C_5$ - $C_6$ -heterocyclo,  $C_5$ - $C_6$ -heteroaryl,  $C_3$ - $C_8$ -cycloalkyl- $C_1$ - $C_6$ -alkyl, aryloxy- $C_1$ - $C_6$ -alkyl, heteroaryloxy- $C_1$ - $C_6$ -alkyl, heteroaryl- $C_1$ - $C_6$ -alkoxy- $C_1$ - $C_6$ -alkyl, heteroarylthio- $C_1$ - $C_6$ -alkyl, arylsulfonyl,  $C_1$ - $C_6$ -alkylsulfonyl,  $C_5$ - $C_6$ -heteroarylsulfonyl, carboxy- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_4$ -alkoxycarbonyl- $C_1$ - $C_6$ -alkyl, aminocarbonyl,  $C_1$ - $C_6$ -alkyl( $R^8N$ )iminocarbonyl, aryl( $R^8N$ )iminocarbonyl,  $C_5$ - $C_6$ -heterocyclo( $R^8N$ )iminocarbonyl, arylthio- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkylthio- $C_1$ - $C_6$ -alkyl, arylthio- $C_3$ - $C_6$ -alkenyl,  $C_1$ - $C_4$ -alkylthio- $C_3$ - $C_6$ -alkenyl,  $C_5$ - $C_6$ -

heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkyl, halo-C<sub>1</sub>-C<sub>6</sub>-alkanoyl, hydroxy-C<sub>1</sub>-C<sub>6</sub>-alkanoyl, thiol-C<sub>1</sub>-C<sub>6</sub>-alkanoyl, C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>3</sub>-C<sub>6</sub>-alkynyl, C<sub>1</sub>-C<sub>4</sub>-alkoxy-C<sub>1</sub>-C<sub>4</sub>-alkyl, C<sub>1</sub>-C<sub>5</sub>-alkoxycarbonyl, aryloxycarbonyl, NR<sup>8</sup>R<sup>9</sup>-

- 5 (R<sup>8</sup>)iminomethyl, NR<sup>8</sup>R<sup>9</sup>-C<sub>1</sub>-C<sub>5</sub>-alkylcarbonyl, hydroxy-C<sub>1</sub>-C<sub>5</sub>-alkyl, R<sup>8</sup>R<sup>9</sup>-aminocarbonyl, R<sup>8</sup>R<sup>9</sup>-aminocarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl, hydroxyaminocarbonyl, R<sup>8</sup>R<sup>9</sup>-aminosulfonyl, R<sup>8</sup>R<sup>9</sup>-aminosulfon-C<sub>1</sub>-C<sub>6</sub>-alkyl, R<sup>8</sup>R<sup>9</sup>-amino-C<sub>1</sub>-C<sub>6</sub>-alkylsulfonyl and an R<sup>8</sup>R<sup>9</sup>-amino-C<sub>1</sub>-C<sub>6</sub>-alkyl group;
- 10

R<sup>7</sup> is selected from the group consisting of a arylalkyl, aryl, heteroaryl, heterocyclo, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub>-alkynyl, C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>1</sub>-C<sub>6</sub>-carboxyalkyl and a C<sub>1</sub>-C<sub>6</sub>-hydroxyalkyl group;

- 15 R<sup>8</sup> and R<sup>9</sup> and R<sup>10</sup> and R<sup>11</sup> are independently selected from the group consisting of a hydrido, hydroxy, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkanoyl, aroyl, aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryl, heteroar-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>2</sub>-C<sub>6</sub>-alkynyl, C<sub>2</sub>-C<sub>6</sub>-alkenyl, thiol-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, cycloalkyl, cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, heterocycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, aralkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxycarbonylar-C<sub>1</sub>-C<sub>6</sub>-alkyl, aminocarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, arylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroarylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, the sulfoxide or
- 20
- 25

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sulfone of any said thio substituents, perfluoro-C<sub>1</sub>-C<sub>6</sub>-alkyl, trifluoromethyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, halo-C<sub>1</sub>-C<sub>6</sub>-alkyl, alkoxycarbonylamino-C<sub>1</sub>-C<sub>6</sub>-alkyl and an amino-C<sub>1</sub>-C<sub>6</sub>-alkyl group wherein the aminoalkyl nitrogen is

5 (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C<sub>1</sub>-C<sub>6</sub>-alkyl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, cycloalkyl and C<sub>1</sub>-C<sub>6</sub>-alkanoyl, or wherein R<sup>8</sup> and R<sup>9</sup> or R<sup>10</sup> and R<sup>11</sup> and the carbon to which they are bonded form a

10 carbonyl group, or wherein R<sup>8</sup> and R<sup>9</sup> or R<sup>10</sup> and R<sup>11</sup>, or R<sup>8</sup> and R<sup>10</sup> together with the atoms to which they are bonded form a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclic or heteroaryl ring containing one or two heteroatoms that are nitrogen,

15 oxygen, or sulfur, with the proviso that only one of R<sup>8</sup> and R<sup>9</sup> or R<sup>10</sup> and R<sup>11</sup> is hydroxy;

R<sup>12</sup> and R<sup>12'</sup> are independently selected from the group consisting of a hydrido, C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryl, heteroaralkyl, C<sub>2</sub>-C<sub>6</sub>-alkynyl, C<sub>2</sub>-C<sub>6</sub>-alkenyl, thiol-C<sub>1</sub>-C<sub>6</sub>-alkyl,

20 cycloalkyl, cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, heterocycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, amino-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxycarbonylar-C<sub>1</sub>-C<sub>6</sub>-alkyl,

25 aminocarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, arylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroarylthio-C<sub>1</sub>-C<sub>6</sub>-

alkyl, the sulfoxide or sulfone of any said thio  
substituents, perfluoro-C<sub>1</sub>-C<sub>6</sub>-alkyl, trifluoromethyl-  
C<sub>1</sub>-C<sub>6</sub>-alkyl, halo-C<sub>1</sub>-C<sub>6</sub>-alkyl, alkoxycarbonylamino-  
C<sub>1</sub>-C<sub>6</sub>-alkyl and an amino-C<sub>1</sub>-C<sub>6</sub>-alkyl group wherein  
5 the aminoalkyl nitrogen is (i) unsubstituted or (ii)  
substituted with one or two radicals independently  
selected from the group consisting of C<sub>1</sub>-C<sub>6</sub>-alkyl,  
ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, cycloalkyl and C<sub>1</sub>-C<sub>6</sub>-alkanoyl; and

R<sup>13</sup> is selected from the group consisting  
10 of a hydrido, benzyl, phenyl, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>2</sub>-C<sub>6</sub>-  
alkynyl, C<sub>2</sub>-C<sub>6</sub>-alkenyl and a C<sub>1</sub>-C<sub>6</sub>-hydroxyalkyl  
group.

63. The compound or salt according to  
15 claim 62 wherein the sum of m + n + p = 1 or 2.

64. The compound or salt according to  
claim 62 wherein Z is O, S or NR<sup>6</sup>.

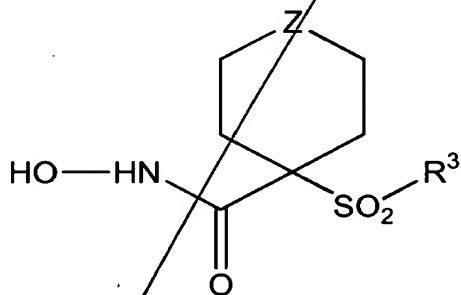
20 65. The compound or salt according to  
claim 62 wherein R<sup>6</sup> is selected from the group  
consisting of C<sub>3</sub>-C<sub>6</sub>-cycloalkyl, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub>-  
alkenyl, C<sub>3</sub>-C<sub>6</sub>-alkynyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl,  
amino-C<sub>1</sub>-C<sub>6</sub>-alkyl, aminosulfonyl, heteroaryl-C<sub>1</sub>-C<sub>6</sub>-  
25 ~~alkyl, aryloxycarbonyl, and C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonyl.~~

66. The compound or salt according to  
claim 62 wherein m = n = ~~zero~~, p = 1, and Y is NR<sup>6</sup>.

*Sub B14* 67. ~~The compound or salt according to~~  
claim 62 wherein R<sup>14</sup> is hydrido.

68. The compound or salt according to claim 62 wherein W of the  $C(W)R^{15}$  is O and  $R^{15}$  is a  $C_1$ - $C_6$ -alkyl, aryl,  $C_1$ - $C_6$ -alkoxy, heteroaryl- $C_1$ - $C_6$ -alkyl,  $C_3$ - $C_8$ -cycloalkyl- $C_1$ - $C_6$ -alkyl, or aryloxy group.

69. A compound corresponding in structure to formula IV, below, or a pharmaceutically acceptable salt thereof



IV

wherein  $R^3$  is a single-ringed aryl or heteroaryl group that is 5- or 6-membered, and is itself substituted at its own 4-position when a 6-membered ring or at its own 3- or 4-position when a 5-membered ring with a substituent selected from the group consisting of one other single-ringed aryl or heteroaryl group, a  $C_3$ - $C_{14}$  alkyl group, a N-piperidyl group, a N-piperazinyl group, a phenoxy group, a thiophenoxy group, a 4-thiopyridyl group, a phenylazo group and a benzamido group; and

$Z$  is selected group the group consisting of O, S,  $NR^6$ , SO,  $SO_2$ , and  $NSO_2R^7$ ,

wherein  $R^6$  is selected from the group consisting of hydrido,  $C_1$ - $C_5$ -alkyl,  $C_1$ - $C_5$ -alkanoyl, benzyl, benzoyl,  $C_3$ - $C_5$ -alkynyl,  $C_3$ - $C_5$ -alkenyl,  $C_1$ - $C_3$ -alkoxy- $C_1$ - $C_4$ -alkyl,  $C_3$ - $C_6$ -cycloalkyl, heteroaryl- $C_1$ -  
5  $C_6$ -alkyl,  $C_1$ - $C_5$ -hydroxyalkyl,  $C_1$ - $C_5$ -carboxyalkyl,  $C_1$ - $C_5$ -alkoxy  $C_1$ - $C_5$ -alkylcarbonyl, and  $NR^8R^9$ - $C_1$ - $C_5$ -alkylcarbonyl or  $NR^8R^9$ - $C_1$ - $C_5$ -alkyl wherein  $R^8$  and  $R^9$  are independently hydrido,  $C_1$ - $C_5$ -alkyl,  $C_1$ - $C_5$ -alkoxycarbonyl or aryl- $C_1$ - $C_5$ -alkoxycarbonyl, or  $NR^8R^9$   
10 together form a heterocyclic ring containing 5- to 8-atoms in the ring; and

$R^7$  is selected from the group consisting of a arylalkyl, aryl, heteroaryl, heterocyclo,  $C_1$ - $C_6$ -alkyl,  $C_3$ - $C_6$ -alkynyl,  $C_3$ - $C_6$ -alkenyl,  $C_1$ - $C_6$ -  
15 carboxyalkyl and a  $C_1$ - $C_6$ -hydroxyalkyl group.

70. The compound or salt according to claim 69 wherein  $R^3$  has a length that is greater than that of a pentyl group and a length that is less than  
20 that of an icosyl group.

71. The compound or salt according to claim 69 wherein Z is O, S or  $NR^6$ .

25 72. The compound or salt according to claim 69 wherein  $R^6$  is selected from the group consisting of  $C_3$ - $C_6$ -cycloalkyl,  $C_1$ - $C_6$ -alkoxy- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkyl,  $C_3$ - $C_6$ -alkenyl,  $C_3$ - $C_6$ -alkynyl,

amino-C<sub>1</sub>-C<sub>6</sub>-alkyl, aminosulfonyl, heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy carbonyl, and C<sub>1</sub>-C<sub>6</sub>-alkoxy carbonyl.

73. The compound or salt according to  
5 claim 69 wherein said R<sup>3</sup> radical is the substituent  
G-A-R-E-Y, wherein

G is an aryl or heteroaryl group;

A is selected from the group

consisting of

- 10 (1) -O-;
- (2) -S-;
- (3) -NR<sup>17</sup>-;
- (4) -CO-N(R<sup>17</sup>) or -N(R<sup>17</sup>)-CO-, wherein R<sup>17</sup>  
is hydrogen, C<sub>1</sub>-C<sub>4</sub>-alkyl, or phenyl;
- 15 (5) -CO-O- or -O-CO-;
- (6) -O-CO-O-;
- (7) -HC=CH-;
- (8) -NH-CO-NH-;
- (9) -C≡C-;
- 20 (10) -NH-CO-O- or -O-CO-NH-;
- (11) -N=N-;
- (12) -NH-NH-; and
- (13) -CS-N(R<sup>18</sup>)- or -N(R<sup>18</sup>)-CS-, wherein  
R<sup>18</sup> is hydrogen C<sub>1</sub>-C<sub>4</sub>-alkyl, or
- 25 phenyl; or
- (14) A is absent and G is bonded directly  
to R;
- R is a moiety selected from the group  
consisting of alkyl, alkoxyalkyl, aryl, heteroaryl,



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cycloalkyl, heterocycloalkyl, aralkyl, heteroaralkyl,  
heterocycloalkylalkyl, cycloalkylalkyl,  
cycloalkoxyalkyl, heterocycloalkoxyalkyl,  
aryloxyalkyl, heteroaryloxyalkyl, arylthioalkyl,  
5 heteroarylthioalkyl, cycloalkylthioalkyl, and a  
heterocycloalkylthioalkyl group wherein the aryl or  
heteroaryl or cycloalkyl or heterocycloalkyl  
substituent is (i) unsubstituted or (ii) substituted  
with one or two radicals selected from the group  
10 consisting of a halo, alkyl, perfluoroalkyl,  
perfluoroalkoxy, perfluoroalkylthio,  
trifluoromethylalkyl, amino, alkoxycarbonylalkyl,  
alkoxy, C<sub>1</sub>-C<sub>2</sub>-alkylene-dioxy, hydroxycarbonylalkyl,  
hydroxycarbonylalkylamino, nitro, hydroxy,  
15 hydroxyalkyl, alkanoylamino, and a alkoxycarbonyl  
group, and R is other than alkyl or alkoxyalkyl when  
A is -O- or -S-;

E is selected from the group consisting of

- (1) -CO(R<sup>19</sup>)- or -(R<sup>19</sup>)CO-, wherein R<sup>19</sup> is  
20 a heterocycloalkyl, or a cycloalkyl  
group;  
(2) -CONH- or -HNCO-; and  
(3) -CO-;  
(4) -SO<sub>2</sub>-R<sup>19</sup>- or -R<sup>19</sup>-SO<sub>2</sub>-;  
25 (5) -SO<sub>2</sub>-;  
(6) -NH-SO<sub>2</sub>- or -SO<sub>2</sub>-NH-; or  
(7) E is absent and R is bonded directly  
to Y; and

Y is absent or is selected from the group  
30 consisting of a hydrido, alkyl, alkoxy, haloalkyl,

aryl, aralkyl, cycloalkyl, heteroaryl, hydroxy,  
aryloxy, aralkoxy, heteroaryloxy, heteroaralkyl,  
perfluoroalkoxy, perfluoroalkylthio,  
trifluoromethylalkyl, alkenyl, heterocycloalkyl,  
5 cycloalkyl, trifluoromethyl, alkoxycarbonyl, and a  
aminoalkyl group, wherein the aryl or heteroaryl or  
heterocycloalkyl group is (i) unsubstituted or (ii)  
substituted with one or two radicals independently  
selected from the group consisting of an alkanoyl,  
10 halo, nitro, aralkyl, aryl, alkoxy, and an amino  
group wherein the amino nitrogen is (i) unsubstituted  
or (ii) substituted with one or two groups  
independently selected from hydrido, alkyl, and an  
aralkyl group.

15

74. The compound or salt according to  
claim 69 wherein said -G-A-R-E-Y substituent contains  
two to four carbocyclic or heterocyclic rings.

20

75. The compound or salt according to  
claim 69 wherein each of the two to four rings is 6-  
membered.

25

76. The compound or salt according to  
claim 69 wherein said -G-A-R-E-Y substituent has a  
length that is greater than a hexyl group and a  
length that is less than that of a stearyl group.

30

77. The compound or salt according to  
claim 69 wherein A is -O- or -S-.

5            79. The compound or salt according to  
claim 69 wherein E is absent.

81. The compound or salt according to claim 69 wherein R<sup>3</sup> is a radical that is comprised of a single-ringed aryl or heteroaryl group that is 5- or 6-membered, and is itself substituted at its own 4-position when a 6-membered ring and at its own 3- or 4-position when a 5-membered ring with a substituent selected from the group consisting of a thiophenoxy, 4-chlorophenoxy, 3-chlorophenoxy, 4-methoxyphenoxy, 3-benzodioxol-5-yloxy, 3,4-dimethylphenoxy, 4-fluorophenoxy, 4-fluorothiophenoxy, phenoxy, 4-trifluoromethoxyphenoxy, 4-trifluoromethylphenoxy, 4-(trifluoromethylthio)phenoxy, 4-(trifluoromethylthio)thiophenoxy, 4-chloro-3-fluorophenoxy, 4-isopropoxyphenoxy, 4-isopropylphenoxy, (2-methyl-1,3-benzothiazol-5-yl)oxy, 4-(1H-imidazol-1-yl)phenoxy, 4-chloro-3-methylphenoxy, 3-methylphenoxy, 4-ethoxyphenoxy, 3,4-difluorophenoxy, 4-chloro-3-methylphenoxy, 4-fluoro-3-chlorophenoxy, 4-(1H-1,2,4-triazol-1-yl)phenoxy,

3,5-difluorophenoxy, 3,4-dichlorophenoxy, 4-cyclopentylphenoxy, 4-bromo-3-methylphenoxy, 4-bromophenoxy, 4-methylthiophenoxy, 4-phenylphenoxy, 4-benzylphenoxy, 6-quinolinylloxy, 4-amino-3-methylphenoxy, 3-methoxyphenoxy, 5,6,7,8-tetrahydro-2-naphthalenyloxy, 3-hydroxymethylphenoxy, N-piperidyl, N-piperazinyl and a 4-benzyloxyphenoxy group.

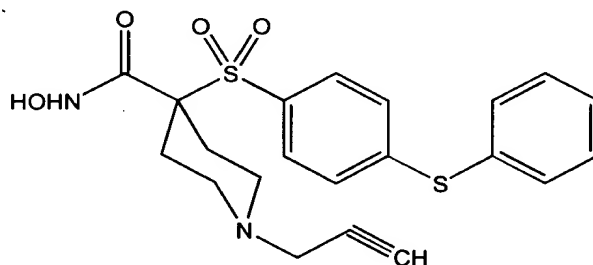
Sub B15/10  
~~82. The compound or salt according to claim 69 wherein said R<sup>3</sup> group is a PhR<sup>23</sup> group, wherein Ph is a phenyl ring that is substituted at its 4-position by an R<sup>23</sup> group that is a substituent selected from the group consisting of another single-  
15 ringed aryl or heteroaryl group, a piperidyl group, a piperazinyl group, a phenoxy group, a thiophenoxy group, a phenylazo group and a benzamido group.~~

~~83. The compound or salt according to  
20 claim 82 wherein said R<sup>23</sup> group is itself substituted with a moiety that is selected from the group consisting of a halogen, a C<sub>1</sub>-C<sub>4</sub> alkoxy group, a C<sub>1</sub>-C<sub>4</sub> alkyl group, a dimethylamino group, a carboxyl C<sub>1</sub>-C<sub>3</sub> alkylene group, a C<sub>1</sub>-C<sub>4</sub> alkoxy carbonyl C<sub>1</sub>-C<sub>3</sub>  
25 alkylene group, a trifluoromethylthio group, a trifluoromethoxy group, a trifluoromethyl group and a carboxamido C<sub>1</sub>-C<sub>3</sub> alkylene group, or is substituted at the meta- and para-positions by a methylenedioxy group.~~

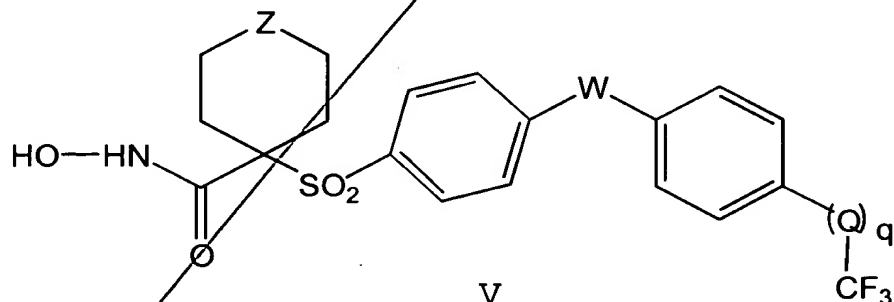
84. The compound or salt according to claim 83 wherein said  $R^{23}$  group is substituted at the para-position.

5 85. The compound or salt according to claim 84 wherein said  $R^{23}$  group is phenoxy.

86. The compound or salt according to claim 69 wherein said inhibitor corresponds in  
10 structure to the formula



66-30-223466  
Sal B16  
87. A compound corresponding in structure to formula V, below, or a pharmaceutically acceptable  
15 salt thereof



20 wherein  
Z is O, S or  $NR^6$ ;

W and Q are independently oxygen (O), NR<sup>6</sup>  
or sulfur (S),

R<sup>6</sup> is selected from the group consisting of  
C<sub>3</sub>-C<sub>6</sub>-cycloalkyl, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>3</sub>-C<sub>6</sub>-  
5 alkynyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, amino-C<sub>1</sub>-C<sub>6</sub>-alkyl,  
aminosulfonyl, heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkyl,  
aryloxycarbonyl, and C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonyl; and

q is zero or one such that when q is zero,  
Q is absent and the trifluoromethyl group is bonded  
10 directly to the depicted phenyl ring.

88. The compound or salt according to  
claim 87 wherein q is zero.

15 89. The compound or salt according to  
claim 87 wherein W is O.

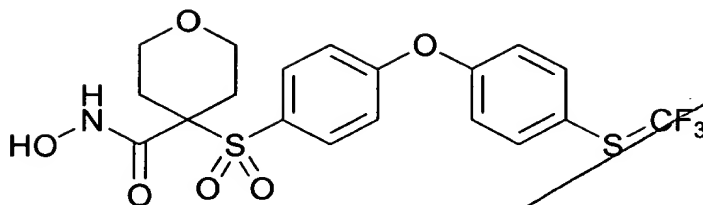
90. The compound or salt according to  
claim 89 wherein q is zero.

20 91. The compound or salt according to  
claim 89 wherein q is one and Q is O.

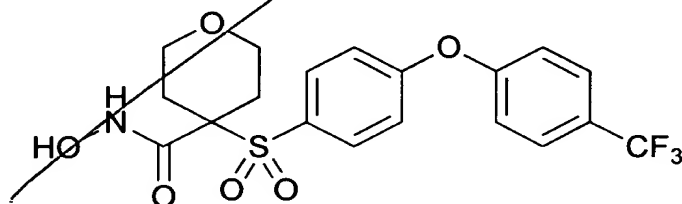
92. The compound or salt according to  
25 claim 89 wherein q is one and Q is S.

93. The compound or salt according to  
claim 87 wherein said inhibitor corresponds in  
structure to the formula

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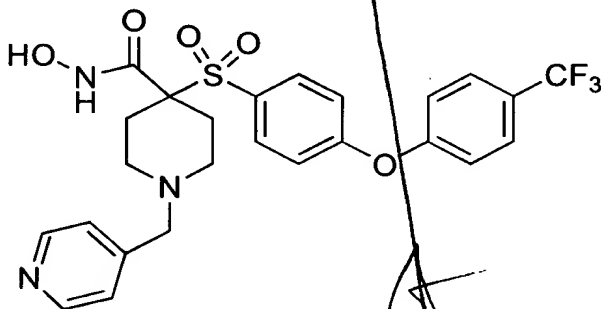


94. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula



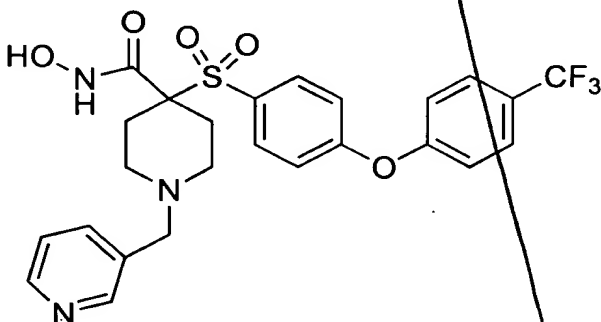
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95. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula

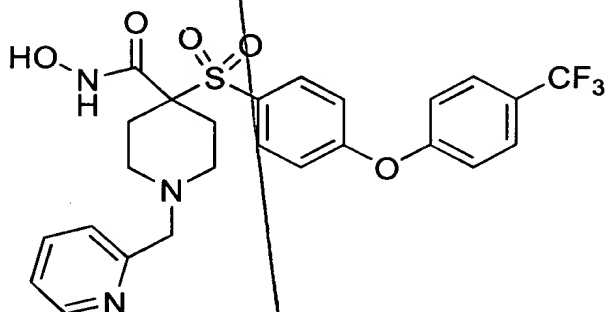


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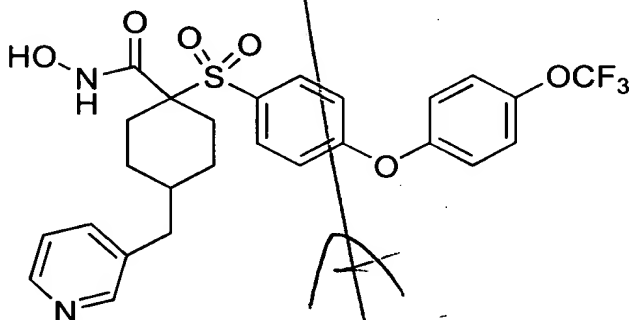
96. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula



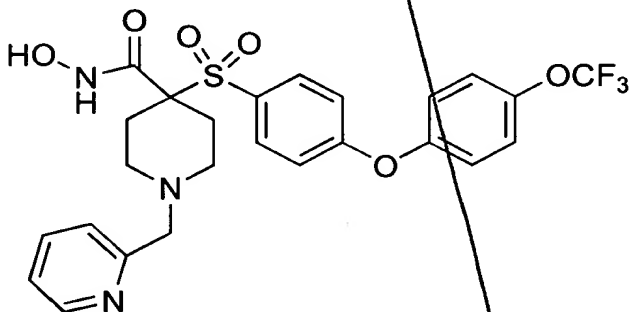
97. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula



5 98. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula

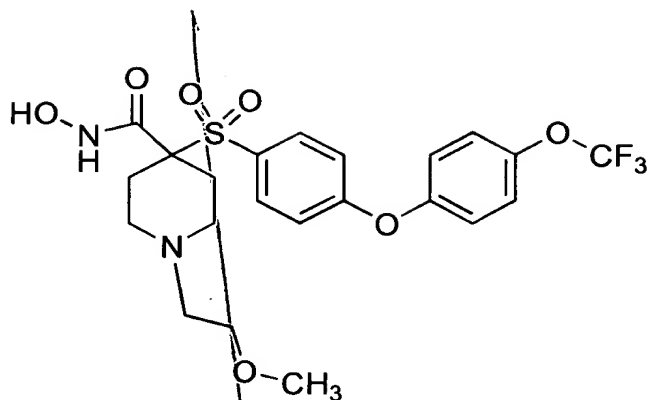


10 99. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula



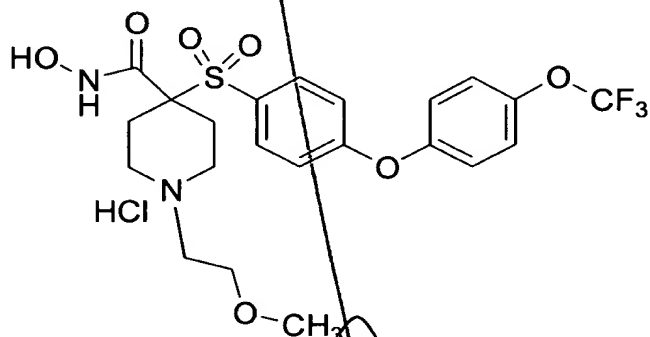
15 100. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula





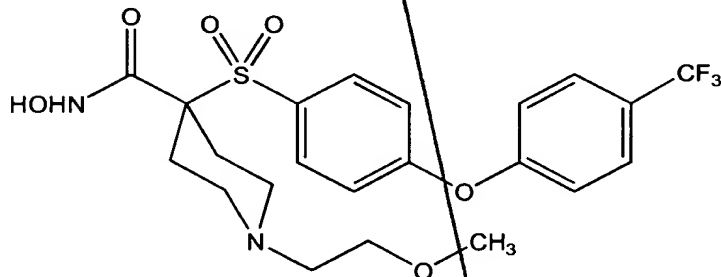
101. The compound or salt according to claim 100 wherein said inhibitor corresponds in structure to the formula

5

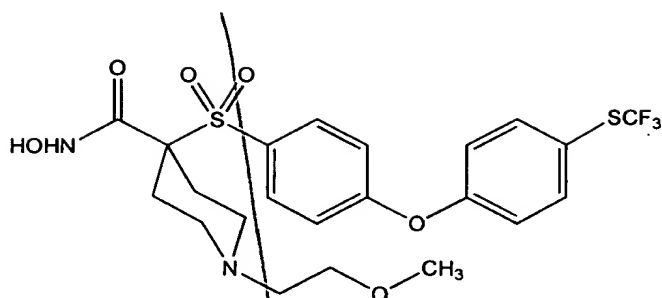


102. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula

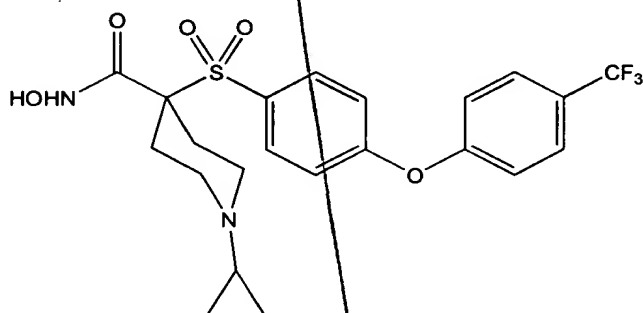
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103. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula

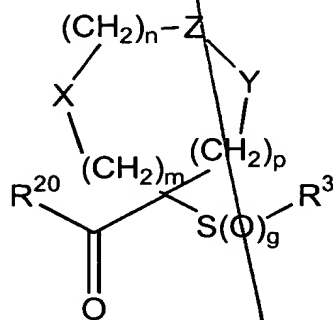


104. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula



5

105. A compound corresponding in structure to formula VI, below



VI

wherein

g is zero, 1 or 2;

15

R<sup>3</sup> is an optionally substituted aryl or optionally substituted heteroaryl radical, and when

said aryl or heteroaryl radical is substituted, the  
substituent is (a) selected from the group consisting  
of an optionally substituted cycloalkyl,  
heterocycloalkyl, aryl, heteroaryl, aralkyl,  
5 heteroaralkyl, aralkoxy, heteroaralkoxy,  
aralkoxyalkyl, aryloxyalkyl, aralkanoylalkyl,  
arylcarbonylalkyl, aralkylaryl, aryloxyalkylaryl,  
aralkoxyaryl, arylazoaryl, arylhydrazinoaryl,  
alkylthioaryl, arylthioalkyl, alkylthioaralkyl,  
10 aralkylthioalkyl, an aralkylthioaryl radical, the  
sulfoxide or sulfone of any of the thio substituents,  
and a fused ring structure comprising two or more 5-  
or 6-membered rings selected from the group  
consisting of aryl, heteroaryl, cycloalkyl and  
15 heterocycloalkyl, and (b) is itself optionally  
substituted with one or more substituents  
independently selected from the group consisting of a  
cyano, perfluoroalkyl, trifluoromethoxy,  
trifluoromethylthio, haloalkyl, trifluoromethylalkyl,  
20 aralkoxycarbonyl, aryloxycarbonyl, hydroxy, halo,  
alkyl, alkoxy, nitro, thiol, hydroxycarbonyl,  
aryloxy, arylthio, aralkyl, aryl, arylcarbonylamino,  
heteroaryloxy, heteroarylthio, heteroaralkyl,  
cycloalkyl, heterocyclooxy, heterocyclothio,  
25 heterocycloamino, cycloalkyloxy, cycloalkylthio,  
heteroaralkoxy, heteroaralkylthio, aralkoxy,  
aralkylthio, aralkylamino, heterocyclo, heteroaryl,  
arylazo, hydroxycarbonylalkoxy, alkoxycarbonylalkoxy,  
alkanoyl, arylcarbonyl, aralkanoyl, alkanoyloxy,  
30 aralkanoyloxy, hydroxyalkyl, hydroxyalkoxy,  
alkylthio, alkoxyalkylthio, alkoxycarbonyl,  
aryloxyalkoxyaryl, arylthioalkylthioaryl,  
aryloxyalkylthioaryl, arylthioalkoxyaryl,

04450 225760

hydroxycarbonylalkoxy, hydroxycarbonylalkylthio,  
alkoxycarbonylalkoxy, alkoxycarbonylalkylthio, amino,

5        wherein the amino nitrogen is (i) unsubstituted,  
      or (ii) substituted with one or two substituents  
      that are independently selected from the group  
      consisting of an alkyl, aryl, heteroaryl,  
      aralkyl, cycloalkyl, aralkoxycarbonyl,  
      alkoxycarbonyl, arylcarbonyl, aralkanoyl,  
      heteroarylcarbonyl, heteroaralkanoyl and an  
10    alkanoyl group, or (iii) wherein the amino  
      nitrogen and two substituents attached thereto  
      form a 5- to 8-membered heterocyclo or  
      heteroaryl ring containing zero to two  
      additional heteroatoms that are nitrogen, oxygen  
15    or sulfur and which ring itself is (a)  
      unsubstituted or (b) substituted with one or two  
      groups independently selected from the group  
      consisting of an aryl, alkyl, heteroaryl,  
      aralkyl, heteroaralkyl, hydroxy, alkoxy,  
20    alkanoyl, cycloalkyl, heterocycloalkyl,  
      alkoxycarbonyl, hydroxyalkyl, trifluoromethyl,  
      benzofused heterocycloalkyl, hydroxyalkoxyalkyl,  
      aralkoxycarbonyl, hydroxycarbonyl,  
      aryloxycarbonyl, benzofused heterocycloalkoxy,  
25    benzofused cycloalkylcarbonyl, heterocyclo-  
      alkylcarbonyl, and a cycloalkylcarbonyl group,  
      carbonylamino

      wherein the carbonylamino nitrogen is (i)  
      unsubstituted, or (ii) is the reacted amine of  
30    an amino acid, or (iii) substituted with one or  
      two radicals selected from the group consisting  
      of an alkyl, hydroxyalkyl, hydroxyheteroaralkyl,  
      cycloalkyl, aralkyl, trifluoromethylalkyl,

heterocycloalkyl, benzofused heterocycloalkyl,  
benzofused heterocycloalkyl, benzofused  
cycloalkyl, and an N,N-dialkylsubstituted  
alkylamino-alkyl group, or (iv) the carboxamido  
5 nitrogen and two substituents bonded thereto  
together form a 5- to 8-membered heterocyclo,  
heteroaryl or benzofused heterocycloalkyl ring  
that is itself unsubstituted or substituted with  
one or two radicals independently selected from  
10 the group consisting of an alkyl,  
alkoxycarbonyl, nitro, heterocycloalkyl,  
hydroxy, hydroxycarbonyl, aryl, aralkyl,  
heteroaralkyl and an amino group,

wherein the amino nitrogen is  
15 (i) unsubstituted, or (ii) substituted with  
one or two substituents that are  
independently selected from the group  
consisting of alkyl, aryl, and heteroaryl,  
or (iii) wherein the amino nitrogen and two  
20 substituents attached thereto form a 5- to  
8-membered heterocyclo or heteroaryl ring,  
and an aminoalkyl group

wherein the aminoalkyl nitrogen is (i)  
unsubstituted, or (ii) substituted with one or two  
25 substituents independently selected from the group  
consisting of an alkyl, aryl, aralkyl, cycloalkyl,  
aralkoxycarbonyl, alkoxycarbonyl, and an alkanoyl  
group, or (iii) wherein the aminoalkyl nitrogen and  
two substituents attached thereto form a 5- to 8-  
30 membered heterocyclo or heteroaryl ring, or is  
an aryl or heteroaryl group that is substituted with  
a nucleophilically displaceable leaving group;

m is zero, 1 or 2;

n is zero, 1 or 2;

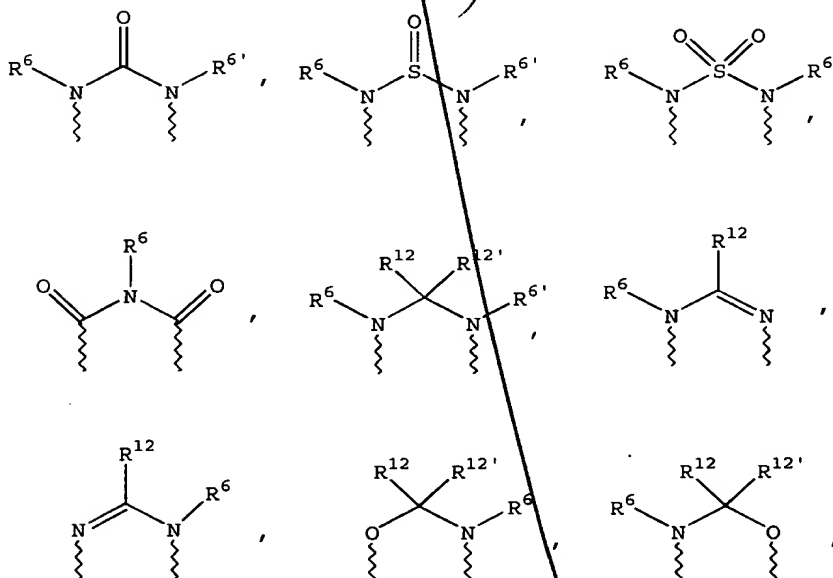
p is zero, 1 or 2;

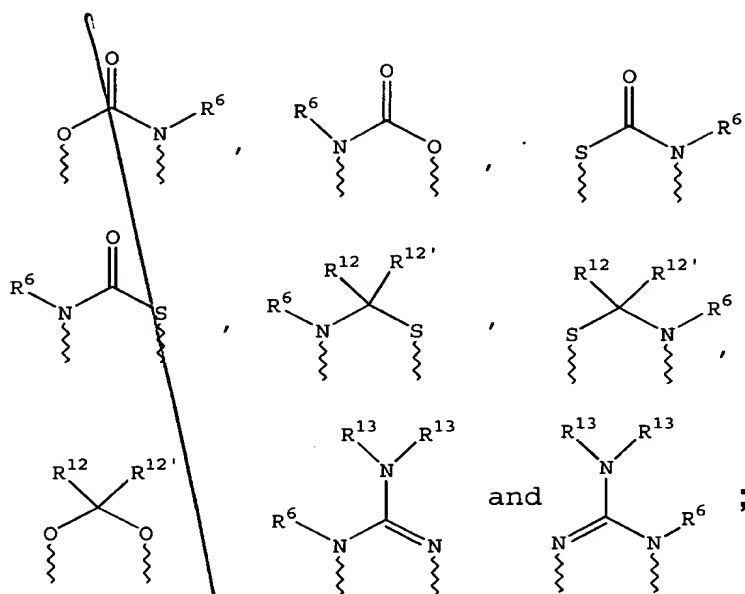
the sum of  $m + n + p = 1, 2, 3$  or 4;

5 (a) one of X, Y and Z is selected from the group consisting of  $C(O)$ ,  $NR^6$ , O, S,  $S(O)$ ,  $S(O)_2$  and  $NS(O)_2R^7$ , and the remaining two of X, Y and Z are  $CR^8R^9$ , and  $CR^{10}R^{11}$ , or

10 (b) X and Z or Z and Y together constitute a moiety that is selected from the group consisting of  $NR^6C(O)$ ,  $NR^6S(O)$ ,  $NR^6S(O)_2$ ,  $NR^6S$ ,  $NR^6O$ , SS,  $NR^6NR^6$  and  $OC(O)$ , with the remaining one of X, Y and Z being  $CR^8R^9$ , or

15 (c) n is zero and X, Y and Z together constitute a moiety selected from the group consisting of





wherein wavy lines are bonds to the atoms of the depicted ring;

- 5  $\text{R}^6$  and  $\text{R}^6'$  are independently selected from the group consisting of hydrido, formyl, sulfonic- $\text{C}_1$ - $\text{C}_6$ -alkyl,  $\text{C}_1$ - $\text{C}_6$ -alkoxycarbonyl- $\text{C}_1$ - $\text{C}_6$ -alkyl, hydroxycarbonyl- $\text{C}_1$ - $\text{C}_6$ -alkyl,  $\text{C}_1$ - $\text{C}_6$ -alkylcarbonyl- $\text{C}_1$ - $\text{C}_6$ -alkyl,  $\text{R}^8\text{R}^9$ -aminocarbonyl- $\text{C}_1$ - $\text{C}_6$ -alkyl,  $\text{C}_1$ - $\text{C}_6$ -alkoxycarbonyl- $\text{C}_1$ - $\text{C}_6$ -alkylcarbonyl, hydroxycarbonyl- $\text{C}_1$ - $\text{C}_6$ -alkylcarbonyl,  $\text{C}_1$ - $\text{C}_6$ -alkylcarbonyl- $\text{C}_1$ - $\text{C}_6$ -alkylcarbonyl,  $\text{C}_1$ - $\text{C}_6$ -alkoxycarbonylcarbonyl, hydroxycarbonylcarbonyl,  $\text{C}_1$ - $\text{C}_6$ -alkylcarbonylcarbonyl,  $\text{R}^8\text{R}^9$ -aminocarbonylcarbonyl,  $\text{C}_1$ - $\text{C}_6$ -alkanoyl, aryl- $\text{C}_1$ - $\text{C}_6$ -alkyl, aroyl, bis( $\text{C}_1$ - $\text{C}_6$ -alkoxy- $\text{C}_1$ - $\text{C}_6$ -alkyl)- $\text{C}_1$ - $\text{C}_6$ -alkyl,  $\text{C}_1$ - $\text{C}_6$ -alkyl,  $\text{C}_1$ - $\text{C}_6$ -haloalkyl,  $\text{C}_1$ - $\text{C}_6$ -perfluoroalkyl,  $\text{C}_1$ - $\text{C}_6$ -trifluoromethylalkyl,  $\text{C}_1$ - $\text{C}_6$ -perfluoroalkoxy- $\text{C}_1$ - $\text{C}_6$ -alkyl,  $\text{C}_1$ - $\text{C}_6$ -alkoxy- $\text{C}_1$ - $\text{C}_6$ -alkyl,  $\text{C}_3$ - $\text{C}_6$ -cycloalkyl, heteroarycarbonyl,
- 10
- 15

heterocyclocarbonyl, C<sub>3</sub>-C<sub>8</sub>-heterocycloalkyl, C<sub>3</sub>-C<sub>8</sub>-  
heterocycloalkylcarbonyl, aryl, C<sub>5</sub>-C<sub>6</sub>-heterocyclo,  
C<sub>5</sub>-C<sub>6</sub>-heteroaryl, C<sub>3</sub>-C<sub>8</sub>-cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl,  
aryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl,  
5 heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroarylthio-  
C<sub>1</sub>-C<sub>6</sub>-alkyl, arylsulfonyl, C<sub>1</sub>-C<sub>6</sub>-alkylsulfonyl, C<sub>5</sub>-  
C<sub>6</sub>-heteroarylsulfonyl, carboxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>4</sub>-  
alkoxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aminocarbonyl, C<sub>1</sub>-C<sub>6</sub>-  
alkyl(R<sup>8</sup>N)iminocarbonyl, aryl(R<sup>8</sup>N)iminocarbonyl, C<sub>5</sub>-  
10 C<sub>6</sub>-heterocyclo(R<sup>8</sup>N)iminocarbonyl, arylthio-C<sub>1</sub>-C<sub>6</sub>-  
alkyl, C<sub>1</sub>-C<sub>6</sub>-alkylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, arylthio-C<sub>3</sub>-C<sub>6</sub>-  
alkenyl, C<sub>1</sub>-C<sub>4</sub>-alkylthio-C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>5</sub>-C<sub>6</sub>-  
heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkyl, halo-C<sub>1</sub>-C<sub>6</sub>-alkanoyl, hydroxy-  
C<sub>1</sub>-C<sub>6</sub>-alkanoyl, thiol-C<sub>1</sub>-C<sub>6</sub>-alkanoyl, C<sub>3</sub>-C<sub>6</sub>-alkenyl,  
15 C<sub>3</sub>-C<sub>6</sub>-alkynyl, C<sub>1</sub>-C<sub>4</sub>-alkoxy-C<sub>1</sub>-C<sub>4</sub>-alkyl, C<sub>1</sub>-C<sub>5</sub>-  
alkoxycarbonyl, aryloxycarbonyl, NR<sup>8</sup>R<sup>9</sup>-  
(R<sup>8</sup>)iminomethyl, NR<sup>8</sup>R<sup>9</sup>-C<sub>1</sub>-C<sub>5</sub>-alkylcarbonyl, hydroxy-  
C<sub>1</sub>-C<sub>5</sub>-alkyl, R<sup>8</sup>R<sup>9</sup>-aminocarbonyl, R<sup>8</sup>R<sup>9</sup>-aminocarbonyl-  
C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl, hydroxyaminocarbonyl, R<sup>8</sup>R<sup>9</sup>-  
20 aminosulfonyl, R<sup>8</sup>R<sup>9</sup>-aminosulfon-C<sub>1</sub>-C<sub>6</sub>-alkyl, R<sup>8</sup>R<sup>9</sup>-  
amino-C<sub>1</sub>-C<sub>6</sub>-alkylsulfonyl and an R<sup>8</sup>R<sup>9</sup>-amino-C<sub>1</sub>-C<sub>6</sub>-  
alkyl group;

R<sup>7</sup> is selected from the group consisting of  
a arylalkyl, aryl, heteroaryl, heterocyclo, C<sub>1</sub>-C<sub>6</sub>-  
25 alkyl, C<sub>3</sub>-C<sub>6</sub>-alkynyl, C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>1</sub>-C<sub>6</sub>-  
carboxyalkyl and a C<sub>1</sub>-C<sub>6</sub>-hydroxyalkyl group;



$R^8$  and  $R^9$  and  $R^{10}$  and  $R^{11}$  are independently selected from the group consisting of a hydrido, hydroxy,  $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkanoyl, aroyl, aryl, ar- $C_1$ - $C_6$ -alkyl, heteroaryl, heteroar- $C_1$ - $C_6$ -alkyl,  $C_2$ - $C_6$ -alkynyl,  $C_2$ - $C_6$ -alkenyl, thiol- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkylthio- $C_1$ - $C_6$ -alkyl, cycloalkyl, cycloalkyl- $C_1$ - $C_6$ -alkyl, heterocycloalkyl- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkoxy- $C_1$ - $C_6$ -alkyl, aralkoxy- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkoxy- $C_1$ - $C_6$ -alkoxy- $C_1$ - $C_6$ -alkyl, hydroxy- $C_1$ - $C_6$ -alkyl, hydroxycarbonyl- $C_1$ - $C_6$ -alkyl, hydroxycarbonylar- $C_1$ - $C_6$ -alkyl, aminocarbonyl- $C_1$ - $C_6$ -alkyl, aryloxy- $C_1$ - $C_6$ -alkyl, heteroaryloxy- $C_1$ - $C_6$ -alkyl, arylthio- $C_1$ - $C_6$ -alkyl, heteroarylthio- $C_1$ - $C_6$ -alkyl, the sulfoxide or sulfone of any said thio substituents, perfluoro- $C_1$ - $C_6$ -alkyl, trifluoromethyl- $C_1$ - $C_6$ -alkyl, halo- $C_1$ - $C_6$ -alkyl, alkoxycarbonylamino- $C_1$ - $C_6$ -alkyl and an amino- $C_1$ - $C_6$ -alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of  $C_1$ - $C_6$ -alkyl, ar- $C_1$ - $C_6$ -alkyl, cycloalkyl and  $C_1$ - $C_6$ -alkanoyl, or wherein  $R^8$  and  $R^9$  or  $R^{10}$  and  $R^{11}$  and the carbon to which they are bonded form a carbonyl group, or wherein  $R^8$  and  $R^9$  or  $R^{10}$  and  $R^{11}$ , or  $R^8$  and  $R^{10}$  together with the atoms to which they are bonded form a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclic or heteroaryl ring containing one or two heteroatoms that are nitrogen,

oxygen, or sulfur, with the proviso that only one of  $R^8$  and  $R^9$  or  $R^{10}$  and  $R^{11}$  is hydroxy;

$R^{12}$  and  $R^{12'}$  are independently selected from the group consisting of a hydrido,  $C_1$ - $C_6$ -alkyl, aryl, ar- $C_1$ - $C_6$ -alkyl, heteroaryl, heteroaralkyl,  $C_2$ - $C_6$ -alkynyl,  $C_2$ - $C_6$ -alkenyl, thiol- $C_1$ - $C_6$ -alkyl, cycloalkyl, cycloalkyl- $C_1$ - $C_6$ -alkyl, heterocycloalkyl- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkoxy- $C_1$ - $C_6$ -alkyl, aryloxy- $C_1$ - $C_6$ -alkyl, amino- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkoxy- $C_1$ - $C_6$ -alkoxy- $C_1$ - $C_6$ -alkyl, hydroxy- $C_1$ - $C_6$ -alkyl, hydroxycarbonyl- $C_1$ - $C_6$ -alkyl, hydroxycarbonylar- $C_1$ - $C_6$ -alkyl, aminocarbonyl- $C_1$ - $C_6$ -alkyl, aryloxy- $C_1$ - $C_6$ -alkyl, heteroaryloxy- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkylthio- $C_1$ - $C_6$ -alkyl, arylthio- $C_1$ - $C_6$ -alkyl, heteroarylthio- $C_1$ - $C_6$ -alkyl, the sulfoxide or sulfone of any said thio substituents, perfluoro- $C_1$ - $C_6$ -alkyl, trifluoromethyl- $C_1$ - $C_6$ -alkyl, halo- $C_1$ - $C_6$ -alkyl, alkoxycarbonylamino- $C_1$ - $C_6$ -alkyl and an amino- $C_1$ - $C_6$ -alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of  $C_1$ - $C_6$ -alkyl, ar- $C_1$ - $C_6$ -alkyl, cycloalkyl and  $C_1$ - $C_6$ -alkanoyl;

$R^{13}$  is selected from the group consisting of a hydrido, benzyl, phenyl,  $C_1$ - $C_6$ -alkyl,  $C_2$ - $C_6$ -alkynyl,  $C_2$ - $C_6$ -alkenyl and a  $C_1$ - $C_6$ -hydroxyalkyl group; and

$R^{20}$  is (a)  $-O-R^{21}$ , wherein  $R^{21}$  is selected from the group consisting of a hydrido,  $C_1$ - $C_6$ -alkyl,

aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl group and a pharmaceutically acceptable cation, (b) -NH-O-R<sup>22</sup>, wherein R<sup>22</sup> is a selectively removable protecting group such as a 2-tetrahydropyranyl, benzyl, p-methoxybenzyl, carbonyl-  
5 C<sub>1</sub>-C<sub>6</sub>-alkoxy, trisubstituted silyl group, an o-nitrophenyl group, and a peptide synthesis resin, wherein the trisubstituted silyl group is substituted with C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, or ar-C<sub>1</sub>-C<sub>6</sub>-alkyl or a mixture thereof, (c) -NH-O-R<sup>14</sup>, where R<sup>14</sup> is hydrido,  
10 a pharmaceutically acceptable cation or C(W)R<sup>25</sup> where W is O or S and R<sup>25</sup> is selected from the group consisting of an C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, C<sub>1</sub>-C<sub>6</sub>-alkoxy, heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>3</sub>-C<sub>8</sub>-cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy, ar-C<sub>1</sub>-C<sub>6</sub>-alkoxy, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryl  
15 and amino C<sub>1</sub>-C<sub>6</sub>-alkyl group wherein the amino C<sub>1</sub>-C<sub>6</sub>-alkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two substituents independently selected from the group consisting of an C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>3</sub>-C<sub>8</sub>-  
20 cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, ar-C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonyl, and C<sub>1</sub>-C<sub>6</sub>-alkanoyl radical, or (iii) wherein the amino C<sub>1</sub>-C<sub>6</sub>-alkyl nitrogen and two substituents attached thereto form a 5- to 8-membered heterocyclo or heteroaryl ring, or (d) -NR<sup>26</sup>R<sup>27</sup>,  
25 where R<sup>26</sup> and R<sup>27</sup> are independently selected from the group consisting of a hydrido, C<sub>1</sub>-C<sub>6</sub>-alkyl, amino C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxy C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl group, or R<sup>26</sup> and R<sup>27</sup> together with the depicted nitrogen atom form a 5- to 8-membered ring

containing zero or one additional heteroatom that is oxygen, nitrogen or sulfur.

106. The compound according to claim 105  
5 wherein  $R^3$  is the substituent G-A-R-E-Y wherein

G is an aryl or heteroaryl group;

A is selected from the group consisting of

(1) -O-;

(2) -S-;

10 (3) -NR<sup>17</sup>-;

(4) -CO-N(R<sup>17</sup>) or -N(R<sup>17</sup>)-CO-, wherein R<sup>17</sup> is hydrogen, C<sub>1</sub>-C<sub>4</sub>-alkyl, or phenyl;

(5) -CO-O- or -O-CO-;

(6) -O-CO-O-;

15 (7) -HC=CH-;

(8) -NH-CO-NH-;

(9) -C≡C-;

(10) -NH-CO-O- or -O-CO-NH-;

(11) -N=N-;

20 (12) -NH-NH-; and

(13) -CS-N(R<sup>18</sup>)- or -N(R<sup>18</sup>)-CS-, wherein R<sup>18</sup> is hydrogen C<sub>1</sub>-C<sub>4</sub>-alkyl, or phenyl; or

25 (14) A is absent and G is bonded directly to R;

R is a moiety selected from the group consisting of alkyl, alkoxyalkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, aralkyl, heteroaralkyl, heterocycloalkylalkyl, cycloalkylalkyl,  
30 cycloalkoxyalkyl, heterocycloalkoxyalkyl,

aryloxyalkyl, heteroaryloxyalkyl, arylthioalkyl, heteroarylthioalkyl, cycloalkylthioalkyl, and a heterocycloalkylthioalkyl group wherein the aryl or heteroaryl or cycloalkyl or heterocycloalkyl

5 substituent is (i) unsubstituted or (ii) substituted with one or two radicals selected from the group consisting of a halo, alkyl, perfluoroalkyl, perfluoroalkoxy, perfluoroalkylthio, trifluoromethylalkyl, amino, alkoxycarbonylalkyl, 10 alkoxy, C<sub>1</sub>-C<sub>2</sub>-alkylene-dioxy, hydroxycarbonylalkyl, hydroxycarbonylalkylamino, nitro, hydroxy, hydroxyalkyl, alkanoylamino, and a alkoxycarbonyl group, and R is other than alkyl or alkoxyalkyl when A is -O- or -S-;

15 E is selected from the group consisting of

- (1) -CO(R<sup>19</sup>)- or -(R<sup>19</sup>)CO-, wherein R<sup>19</sup> is a heterocycloalkyl, or a cycloalkyl group;
- (2) -CONH- or -HNCO-; and
- 20 (3) -CO-;
- (4) -SO<sub>2</sub>-R<sup>19</sup>- or -R<sup>19</sup>-SO<sub>2</sub>-;
- (5) -SO<sub>2</sub>-;
- (6) -NH-SO<sub>2</sub>- or -SO<sub>2</sub>-NH-; or
- (7) E is absent and R is bonded directly 25 to Y; and

Y is absent or is selected from the group consisting of a hydrido, alkyl, alkoxy, haloalkyl, aryl, aralkyl, cycloalkyl, heteroaryl, hydroxy, aryloxy, aralkoxy, heteroaryloxy, heteroaralkyl, 30 perfluoroalkoxy, perfluoroalkylthio,

trifluoromethylalkyl, alkenyl, heterocycloalkyl,  
cycloalkyl, trifluoromethyl, alkoxycarbonyl, and a  
aminoalkyl group, wherein the aryl or heteroaryl or  
heterocycloalkyl group is (i) unsubstituted or (ii)  
5 substituted with one or two radicals independently  
selected from the group consisting of an alkanoyl,  
halo, nitro, aralkyl, aryl, alkoxy, and an amino  
group wherein the amino nitrogen is (i) unsubstituted  
or (ii) substituted with one or two groups  
10 independently selected from hydrido, alkyl, and an  
aralkyl group.

107. The compound according to claim 106  
wherein said -G-A-R-E-Y substituent contains two to  
15 four carbocyclic or heterocyclic rings.

108. The compound according to claim 107  
wherein each of the two to four rings is 6-membered.

20 109. The compound according to claim 106  
wherein said -G-A-R-E-Y substituent has a length that  
is greater than a hexyl group and a length that is  
less than that of a stearyl group.

25 110. The compound according to claim 106  
wherein A is -O- or -S-.

111. The compound according to claim 106  
wherein R is an aryl, heteroaryl, cycloalkyl or  
30 heterocycloalkyl group.

112. The compound according to claim 106 wherein E is absent.

113. The compound according to claim 106  
5 wherein Y is selected from the group consisting of hydrido, an alkyl, alkoxy, perfluoroalkoxy and a perfluoroalkylthio group.

114. The compound according to claim 105  
10 wherein  $R^{14}$  is hydrido.

115. The compound according to claim 105 wherein W of the  $C(W)R^{25}$  is O and  $R^{25}$  is a  $C_1-C_6$ -alkyl, aryl,  $C_1-C_6$ -alkoxy, heteroaryl- $C_1-C_6$ -alkyl,  
15  $C_3-C_8$ -cycloalkyl- $C_1-C_6$ -alkyl, or aryloxy group.

116. The compound according to claim 105 wherein  $R^3$  is a single-ringed aryl or heteroaryl group that is 5- or 6-membered, and is itself  
20 substituted at its own 4-position when a 6-membered ring and at its own 3- or 4-position when a 5-membered ring with a substituent selected from the group consisting of a thiophenoxy, 4-chloro-phenoxy, 3-chlorophenoxy, 4-methoxyphenoxy, 3-benzodioxol-5-yloxy, 3,4-dimethylphenoxy, 4-fluorophenoxy, 4-fluorothiophenoxy, phenoxy, 4-trifluoro-methoxyphenoxy, 4-trifluoromethylphenoxy, 4-(trifluoromethylthio)phenoxy, 4-(trifluoromethylthio)thiophenoxy, 4-chloro-3-fluorophenoxy, 4-isopropoxyphenoxy, 4-isopropylphenoxy, (2-methyl-1,3-benzothiazol-5-yl)oxy, 4-(1H-imidazol-1-yl)phenoxy,  
25  
30

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4-chloro-3-methylphenoxy, 3-methyl-phenoxy, 4-ethoxyphenoxy, 3,4-difluorophenoxy, 4-chloro-3-methylphenoxy, 4-fluoro-3-chlorophenoxy, 4-(1H-1,2,4-triazol-1-yl)phenoxy, 3,5-difluorophenoxy, 3,4-dichlorophenoxy, 4-cyclopentylphenoxy, 4-bromo-3-methylphenoxy, 4-bromophenoxy, 4-methylthiophenoxy, 4-phenylphenoxy, 4-benzylphenoxy, 6-quinolinyloxy, 4-amino-3-methylphenoxy, 3-methoxyphenoxy, 5,6,7,8-tetrahydro-2-naphthalenyloxy, 3-hydroxymethylphenoxy, and a 4-benzyloxyphenoxy group.

117. The compound according to claim 105 wherein said selectively removable protecting group is selected from the group consisting of a 2-tetrahydropyranyl, benzyl, p-methoxybenzyloxy-carbonyl, benzyloxycarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-CH<sub>2</sub>- , C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkoxy-CH<sub>2</sub>- and an o-nitrophenyl group.

118. The compound according to claim 105 wherein said nucleophilically displaceable leaving group is selected from the group consisting of a halo, nitro, azido, phenylsulfoxido, aryloxy, C<sub>1</sub>-C<sub>6</sub>-alkoxy, a C<sub>1</sub>-C<sub>6</sub>-alkylsulfonate or arylsulfonate group and a trisubstituted ammonium group in which the three substituents are independently aryl, ar- C<sub>1</sub>-C<sub>6</sub>-alkyl or C<sub>1</sub>-C<sub>6</sub>-alkyl.

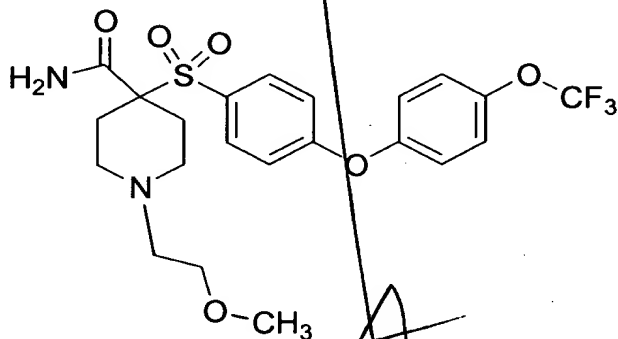
119. The compound according to claim 105 wherein g is zero.



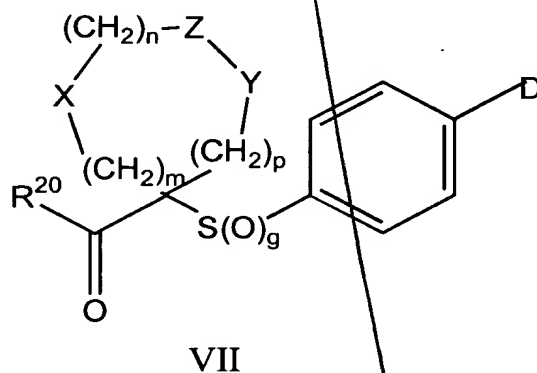
120. The compound according to claim 105 wherein  $R^{20}$  is  $-NR^{26}R^{27}$ .

121. The compound according to claim 120 wherein  $R^{26}$  and  $R^{27}$  are both hydrido.

122. A compound that corresponds in structure to the formula below, or a pharmaceutically acceptable salt thereof



123. An intermediate compound that corresponds in structure to formula VII, below



wherein  
g is zero, 1 or 2;

D is a nucleophilically displaceable leaving group;

m is zero, 1 or 2;

n is zero, 1 or 2;

5 p is zero, 1 or 2;

the sum of  $m + n + p = 1, 2, 3$  or 4;

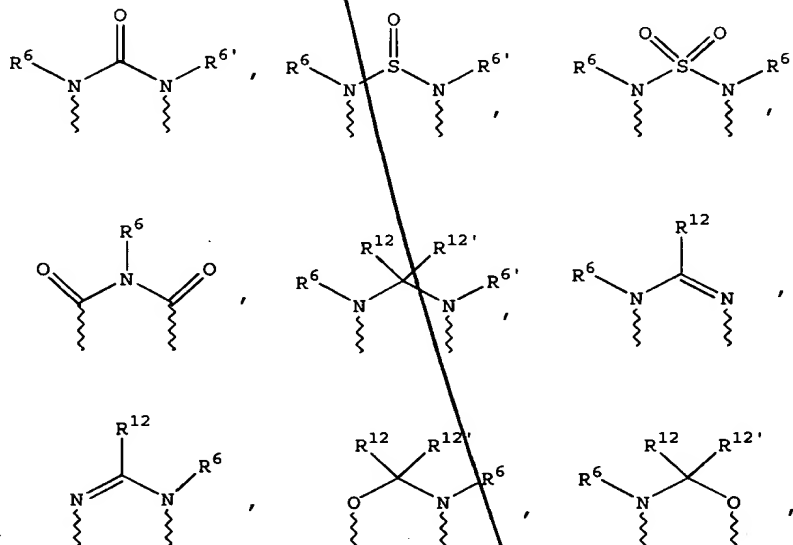
(a) one of X, Y and Z is selected from the group consisting of  $C(O)$ ,  $NR^6$ , O, S,  $S(O)$ ,  $S(O)_2$  and  $NS(O)_2R^7$ , and the remaining two of X, Y and Z are

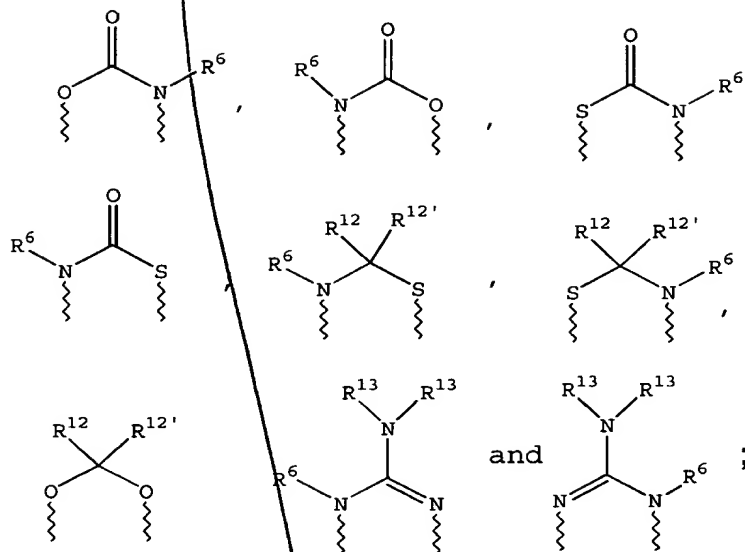
10  $CR^8R^9$ , and  $CR^{10}R^{11}$ , or

(b) X and Z or Z and Y together constitute a moiety that is selected from the group consisting of  $NR^6C(O)$ ,  $NR^6S(O)$ ,  $NR^6S(O)_2$ ,  $NR^6S$ ,  $NR^6O$ , SS,  $NR^6NR^6$  and  $OC(O)$ , with the remaining one of X, Y and Z being  $CR^8R^9$ , or

15 and Z being  $CR^8R^9$ , or

(c) n is zero and X, Y and Z together constitute a moiety selected from the group consisting of





wherein wavy lines are bonds to the atoms of the depicted ring;

- 5  $\text{R}^6$  and  $\text{R}^{6'}$  are independently selected from the group consisting of hydrido, formyl, sulfonic- $\text{C}_1$ - $\text{C}_6$ -alkyl,  $\text{C}_1$ - $\text{C}_6$ -alkoxycarbonyl- $\text{C}_1$ - $\text{C}_6$ -alkyl, hydroxycarbonyl- $\text{C}_1$ - $\text{C}_6$ -alkyl,  $\text{C}_1$ - $\text{C}_6$ -alkylcarbonyl- $\text{C}_1$ - $\text{C}_6$ -alkyl,  $\text{R}^8\text{R}^9$ -aminocarbonyl- $\text{C}_1$ - $\text{C}_6$ -alkyl,  $\text{C}_1$ - $\text{C}_6$ -alkoxycarbonyl- $\text{C}_1$ - $\text{C}_6$ -alkylcarbonyl, hydroxycarbonyl- $\text{C}_1$ - $\text{C}_6$ -alkylcarbonyl,  $\text{C}_1$ - $\text{C}_6$ -alkylcarbonyl- $\text{C}_1$ - $\text{C}_6$ -alkylcarbonyl,  $\text{C}_1$ - $\text{C}_6$ -alkoxycarbonylcarbonyl, hydroxycarbonylcarbonyl,  $\text{C}_1$ - $\text{C}_6$ -alkylcarbonylcarbonyl,  $\text{R}^8\text{R}^9$ -aminocarbonylcarbonyl,  $\text{C}_1$ - $\text{C}_6$ -alkanoyl, aryl- $\text{C}_1$ - $\text{C}_6$ -alkyl, aroyl, bis( $\text{C}_1$ - $\text{C}_6$ -alkoxy- $\text{C}_1$ - $\text{C}_6$ -alkyl)- $\text{C}_1$ - $\text{C}_6$ -alkyl,  $\text{C}_1$ - $\text{C}_6$ -alkyl,  $\text{C}_1$ - $\text{C}_6$ -haloalkyl,  $\text{C}_1$ - $\text{C}_6$ -perfluoroalkyl,  $\text{C}_1$ - $\text{C}_6$ -trifluoromethylalkyl,  $\text{C}_1$ - $\text{C}_6$ -perfluoroalkoxy- $\text{C}_1$ - $\text{C}_6$ -alkyl,  $\text{C}_1$ - $\text{C}_6$ -alkoxy- $\text{C}_1$ - $\text{C}_6$ -alkyl,  $\text{C}_3$ - $\text{C}_6$ -cycloalkyl, heteroarycarbonyl,
- 10
- 15

heterocyclocarbonyl, C<sub>3</sub>-C<sub>8</sub>-heterocycloalkyl, C<sub>3</sub>-C<sub>8</sub>-  
heterocycloalkylcarbonyl, aryl, C<sub>5</sub>-C<sub>6</sub>-heterocyclo,  
C<sub>5</sub>-C<sub>6</sub>-heteroaryl, C<sub>3</sub>-C<sub>8</sub>-cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl,  
aryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl,  
5 heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroarylthio-  
C<sub>1</sub>-C<sub>6</sub>-alkyl, arylsulfonyl, C<sub>1</sub>-C<sub>6</sub>-alkylsulfonyl, C<sub>5</sub>-  
C<sub>6</sub>-heteroarylsulfonyl, carboxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>4</sub>-  
alkoxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aminocarbonyl, C<sub>1</sub>-C<sub>6</sub>-  
alkyl(R<sup>8</sup>N)iminocarbonyl, aryl(R<sup>8</sup>N)iminocarbonyl, C<sub>5</sub>-  
10 C<sub>6</sub>-heterocyclo(R<sup>8</sup>N)iminocarbonyl, arylthio-C<sub>1</sub>-C<sub>6</sub>-  
alkyl, C<sub>1</sub>-C<sub>6</sub>-alkylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, arylthio-C<sub>3</sub>-C<sub>6</sub>-  
alkenyl, C<sub>1</sub>-C<sub>4</sub>-alkylthio-C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>5</sub>-C<sub>6</sub>-  
heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkyl, halo-C<sub>1</sub>-C<sub>6</sub>-alkanoyl, hydroxy-  
C<sub>1</sub>-C<sub>6</sub>-alkanoyl, thiol-C<sub>1</sub>-C<sub>6</sub>-alkanoyl, C<sub>3</sub>-C<sub>6</sub>-alkenyl,  
15 C<sub>3</sub>-C<sub>6</sub>-alkynyl, C<sub>1</sub>-C<sub>4</sub>-alkoxy-C<sub>1</sub>-C<sub>4</sub>-alkyl, C<sub>1</sub>-C<sub>5</sub>-  
alkoxycarbonyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, NR<sup>8</sup>R<sup>9</sup>-  
(R<sup>8</sup>)iminomethyl, NR<sup>8</sup>R<sup>9</sup>-C<sub>1</sub>-C<sub>5</sub>-alkylcarbonyl, hydroxy-  
C<sub>1</sub>-C<sub>5</sub>-alkyl, R<sup>8</sup>R<sup>9</sup>-aminocarbonyl, R<sup>8</sup>R<sup>9</sup>-aminocarbonyl-  
C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl, hydroxyaminocarbonyl, R<sup>8</sup>R<sup>9</sup>-  
20 aminosulfonyl, R<sup>8</sup>R<sup>9</sup>-aminosulfon-C<sub>1</sub>-C<sub>6</sub>-alkyl, R<sup>8</sup>R<sup>9</sup>-  
amino-C<sub>1</sub>-C<sub>6</sub>-alkylsulfonyl and an R<sup>8</sup>R<sup>9</sup>-amino-C<sub>1</sub>-C<sub>6</sub>-  
alkyl group;

R<sup>7</sup> is selected from the group consisting of  
a arylalkyl, aryl, heteroaryl, heterocyclo, C<sub>1</sub>-C<sub>6</sub>-  
25 alkyl, C<sub>3</sub>-C<sub>6</sub>-alkynyl, C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>1</sub>-C<sub>6</sub>-  
carboxyalkyl and a C<sub>1</sub>-C<sub>6</sub>-hydroxyalkyl group;

5 R<sup>8</sup> and R<sup>9</sup> and R<sup>10</sup> and R<sup>11</sup> are independently selected from the group consisting of a hydrido, hydroxy, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkanoyl, aroyl, aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryl, heteroar-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>2</sub>-C<sub>6</sub>-alkynyl, C<sub>2</sub>-C<sub>6</sub>-alkenyl, thiol-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, cycloalkyl, cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, heterocycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, aralkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxycarbonylar-C<sub>1</sub>-C<sub>6</sub>-alkyl, aminocarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, arylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroarylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, the sulfoxide or sulfone of any said thio substituents, perfluoro-C<sub>1</sub>-C<sub>6</sub>-alkyl, trifluoromethyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, halo-C<sub>1</sub>-C<sub>6</sub>-alkyl, alkoxy-carbonylamino-C<sub>1</sub>-C<sub>6</sub>-alkyl and an amino-C<sub>1</sub>-C<sub>6</sub>-alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C<sub>1</sub>-C<sub>6</sub>-alkyl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, cycloalkyl and C<sub>1</sub>-C<sub>6</sub>-alkanoyl, or wherein R<sup>8</sup> and R<sup>9</sup> or R<sup>10</sup> and R<sup>11</sup> and the carbon to which they are bonded form a carbonyl group, or wherein R<sup>8</sup> and R<sup>9</sup> or R<sup>10</sup> and R<sup>11</sup>, or R<sup>8</sup> and R<sup>10</sup> together with the atoms to which they are bonded form a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclic or heteroaryl ring containing one or two heteroatoms that are nitrogen,

oxygen, or sulfur, with the proviso that only one of  $R^8$  and  $R^9$  or  $R^{10}$  and  $R^{11}$  is hydroxy;

$R^{12}$  and  $R^{12'}$  are independently selected from the group consisting of a hydrido,  $C_1$ - $C_6$ -alkyl, aryl, ar- $C_1$ - $C_6$ -alkyl, heteroaryl, heteroaralkyl,  $C_2$ - $C_6$ -alkynyl,  $C_2$ - $C_6$ -alkenyl, thiol- $C_1$ - $C_6$ -alkyl, cycloalkyl, cycloalkyl- $C_1$ - $C_6$ -alkyl, heterocycloalkyl- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkoxy- $C_1$ - $C_6$ -alkyl, aryloxy- $C_1$ - $C_6$ -alkyl, amino- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkoxy- $C_1$ - $C_6$ -alkoxy- $C_1$ - $C_6$ -alkyl, hydroxy- $C_1$ - $C_6$ -alkyl, hydroxycarbonyl- $C_1$ - $C_6$ -alkyl, hydroxycarbonylar- $C_1$ - $C_6$ -alkyl, aminocarbonyl- $C_1$ - $C_6$ -alkyl, aryloxy- $C_1$ - $C_6$ -alkyl, heteroaryloxy- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkylthio- $C_1$ - $C_6$ -alkyl, arylthio- $C_1$ - $C_6$ -alkyl, heteroarylthio- $C_1$ - $C_6$ -alkyl, the sulfoxide or sulfone of any said thio substituents, perfluoro- $C_1$ - $C_6$ -alkyl, trifluoromethyl- $C_1$ - $C_6$ -alkyl, halo- $C_1$ - $C_6$ -alkyl, alkoxycarbonylamino- $C_1$ - $C_6$ -alkyl and an amino- $C_1$ - $C_6$ -alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of  $C_1$ - $C_6$ -alkyl, ar- $C_1$ - $C_6$ -alkyl, cycloalkyl and  $C_1$ - $C_6$ -alkanoyl;

$R^{13}$  is selected from the group consisting of a hydrido, benzyl, phenyl,  $C_1$ - $C_6$ -alkyl,  $C_2$ - $C_6$ -alkynyl,  $C_2$ - $C_6$ -alkenyl and a  $C_1$ - $C_6$ -hydroxyalkyl group; and

$R^{20}$  is (a)  $-O-R^{21}$ , wherein  $R^{21}$  is selected from the group consisting of a hydrido,  $C_1$ - $C_6$ -alkyl,

aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl group and a pharmaceutically acceptable cation, (b) -NH-O-R<sup>22</sup>, wherein R<sup>22</sup> is a selectively removable protecting group such as a 2-tetrahydropyranyl, benzyl, p-methoxybenzyl, carbonyl-  
5 C<sub>1</sub>-C<sub>6</sub>-alkoxy, trisubstituted silyl group, an o-nitrophenyl group, and a peptide synthesis resin, wherein the trisubstituted silyl group is substituted with C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, or ar-C<sub>1</sub>-C<sub>6</sub>-alkyl or a mixture thereof, (c) -NH-O-R<sup>14</sup>, where R<sup>14</sup> is hydrido,  
10 a pharmaceutically acceptable cation or C(W)R<sup>25</sup> where W is O or S and R<sup>25</sup> is selected from the group consisting of an C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, C<sub>1</sub>-C<sub>6</sub>-alkoxy, heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>3</sub>-C<sub>8</sub>-cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy, ar-C<sub>1</sub>-C<sub>6</sub>-alkoxy, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryl  
15 and amino C<sub>1</sub>-C<sub>6</sub>-alkyl group wherein the amino C<sub>1</sub>-C<sub>6</sub>-alkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two substituents independently selected from the group consisting of an C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>3</sub>-C<sub>8</sub>-  
20 cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, ar-C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonyl, and C<sub>1</sub>-C<sub>6</sub>-alkanoyl radical, or (iii) wherein the amino C<sub>1</sub>-C<sub>6</sub>-alkyl nitrogen and two substituents attached thereto form a 5- to 8-membered heterocyclo or heteroaryl ring, or (d) -NR<sup>26</sup>R<sup>27</sup>,  
25 where R<sup>26</sup> and R<sup>27</sup> are independently selected from the group consisting of a hydrido, C<sub>1</sub>-C<sub>6</sub>-alkyl, amino C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxy C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl group, or R<sup>26</sup> and R<sup>27</sup> together with the depicted nitrogen atom form a 5- to 8-membered ring containing

zero or one additional heteroatom that is oxygen, nitrogen or sulfur.

124. The compound according to claim 123  
5 wherein said selectively removable protecting group is selected from the group consisting of a 2-tetrahydropyranyl, C<sub>1</sub>-C<sub>6</sub>-acyl, aroyl, benzyl, p-methoxybenzyloxycarbonyl, benzyloxycarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-CH<sub>2</sub>-, C<sub>1</sub>-C<sub>6</sub>-alkoxy-  
10 C<sub>1</sub>-C<sub>6</sub>-alkoxy-CH<sub>2</sub>- and an o-nitrophenyl group.

125. The compound according to claim 123 wherein said nucleophilically displaceable leaving group, D, is selected from the group consisting of a  
15 halo, nitro, azido, phenylsulfoxido, aryloxy, C<sub>1</sub>-C<sub>6</sub>-alkoxy, a C<sub>1</sub>-C<sub>6</sub>-alkylsulfonate or arylsulfonate group and a trisubstituted ammonium group in which the three substituents are independently aryl, ar- C<sub>1</sub>-C<sub>6</sub>-alkyl or C<sub>1</sub>-C<sub>6</sub>-alkyl.

20

126. The compound according to claim 123 wherein said halo group is fluoro.

127. The compound according to claim 123  
25 wherein g is zero.

*Sub B17* ~~128. A pharmaceutical composition that~~  
comprises a compound according to claim 52 dissolved or dispersed in a pharmaceutically acceptable  
30 carrier.

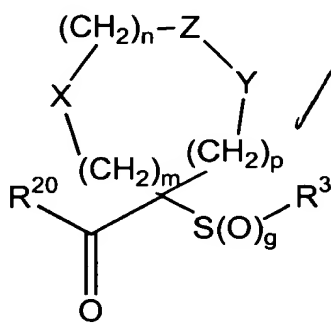


129. A pharmaceutical composition that comprises a compound according to claim 62 dissolved or dispersed in a pharmaceutically acceptable carrier.

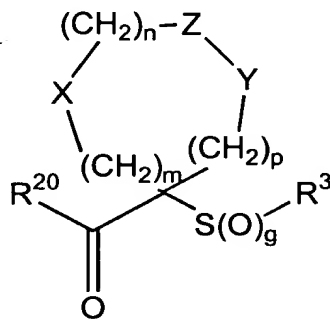
130. A pharmaceutical composition that comprises a compound according to claim 69 dissolved or dispersed in a pharmaceutically acceptable carrier.

131. A pharmaceutical composition that comprises a compound according to claim 87 dissolved or dispersed in a pharmaceutically acceptable carrier.

132. A process for forming a metalloprotease inhibitor compound product or intermediate compound product therefore that comprises the step of coupling an intermediate compound with another moiety, wherein said intermediate compound corresponds in structure to formula VIB, below, and said product corresponds in structure to formula VIA, below:



VIA



VIB

wherein

g is zero, 1 or 2;

R<sup>3'</sup> is an aryl or heteroaryl group that is substituted with a coupling substituent reactive for coupling with another moiety ;

5 R<sup>3</sup> is an optionally substituted aryl or optionally substituted heteroaryl radical, and when said aryl or heteroaryl radical is substituted, the substituent is (a) selected from the group consisting of an optionally substituted cycloalkyl,  
10 heterocycloalkyl, aryl, heteroaryl, aralkyl, heteroaralkyl, aralkoxy, heteroaralkoxy, aralkoxyalkyl, aryloxyalkyl, aralkanoylalkyl, arylcarbonylalkyl, aralkylaryl, aryloxyalkylaryl, aralkoxyaryl, arylazoaryl, arylhydrazinoaryl,  
15 alkylthioaryl, arylthioalkyl, alkylthioaralkyl, aralkylthioalkyl, an aralkylthioaryl radical, the sulfoxide or sulfone of any of the thio substituents, and a fused ring structure comprising two or more 5- or 6-membered rings selected from the group  
20 consisting of aryl, heteroaryl, cycloalkyl and heterocycloalkyl, and (b) is itself optionally substituted with one or more substituents independently selected from the group consisting of a cyano, perfluoroalkyl, trifluoromethoxy,  
25 trifluoromethylthio, haloalkyl, trifluoromethylalkyl, aralkoxycarbonyl, aryloxycarbonyl, hydroxy, halo, alkyl, alkoxy, nitro, thiol, hydroxycarbonyl, aryloxy, arylthio, aralkyl, aryl, arylcarbonylamino, heteroaryloxy, heteroarylthio, heteroaralkyl,  
30 cycloalkyl, heterocyclooxy, heterocyclothio, heterocycloamino, cycloalkyloxy, cycloalkylthio, heteroaralkoxy, heteroaralkylthio, aralkoxy,

aralkylthio, aralkylamino, heterocyclo, heteroaryl,  
arylazo, hydroxycarbonylalkoxy, alkoxycarbonylalkoxy,  
alkanoyl, arylcarbonyl, aralkanoyl, alkanoyloxy,  
aralkanoyloxy, hydroxyalkyl, hydroxyalkoxy,  
5 alkylthio, alkoxylalkylthio, alkoxycarbonyl,  
aryloxyalkoxyaryl, arylthioalkylthioaryl,  
aryloxyalkylthioaryl, arylthioalkoxyaryl,  
hydroxycarbonylalkoxy, hydroxycarbonylalkylthio,  
alkoxycarbonylalkoxy, alkoxycarbonylalkylthio, amino,  
10 wherein the amino nitrogen is (i) unsubstituted,  
or (ii) substituted with one or two substituents  
that are independently selected from the group  
consisting of an alkyl, aryl, heteroaryl,  
aralkyl, cycloalkyl, aralkoxycarbonyl,  
15 alkoxycarbonyl, arylcarbonyl, aralkanoyl,  
heteroarylcarbonyl, heteroaralkanoyl and an  
alkanoyl group, or (iii) wherein the amino  
nitrogen and two substituents attached thereto  
form a 5- to 8-membered heterocyclo or  
20 heteroaryl ring containing zero to two  
additional heteroatoms that are nitrogen, oxygen  
or sulfur and which ring itself is (a)  
unsubstituted or (b) substituted with one or two  
groups independently selected from the group  
25 consisting of an aryl, alkyl, heteroaryl,  
aralkyl, heteroaralkyl, hydroxy, alkoxy,  
alkanoyl, cycloalkyl, heterocycloalkyl,  
alkoxycarbonyl, hydroxyalkyl, trifluoromethyl,  
benzofused heterocycloalkyl, hydroxyalkoxyalkyl,  
30 aralkoxycarbonyl, hydroxycarbonyl,  
aryloxycarbonyl, benzofused heterocycloalkoxy,  
benzofused cycloalkylcarbonyl, heterocyclo-  
alkylcarbonyl, and a cycloalkylcarbonyl group,

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carbonylamino

wherein the carbonylamino nitrogen is (i)  
unsubstituted, or (ii) is the reacted amine of  
an amino acid, or (iii) substituted with one or  
5 two radicals selected from the group consisting  
of an alkyl, hydroxyalkyl, hydroxyheteroaralkyl,  
cycloalkyl, aralkyl, trifluoromethylalkyl,  
heterocycloalkyl, benzofused heterocycloalkyl,  
benzofused heterocycloalkyl, benzofused  
10 cycloalkyl, and an N,N-dialkylsubstituted  
alkylamino-alkyl group, or (iv) the carboxamido  
nitrogen and two substituents bonded thereto  
together form a 5- to 8-membered heterocyclo,  
heteroaryl or benzofused heterocycloalkyl ring  
15 that is itself unsubstituted or substituted with  
one or two radicals independently selected from  
the group consisting of an alkyl,  
alkoxycarbonyl, nitro, heterocycloalkyl,  
hydroxy, hydroxycarbonyl, aryl, aralkyl,  
20 heteroaralkyl and an amino group,

wherein the amino nitrogen is  
(i) unsubstituted, or (ii) substituted with  
one or two substituents that are  
independently selected from the group  
25 consisting of alkyl, aryl, and heteroaryl,  
or (iii) wherein the amino nitrogen and two  
substituents attached thereto form a 5- to  
8-membered heterocyclo or heteroaryl ring,  
and an aminoalkyl group

30 wherein the aminoalkyl nitrogen is (i)  
unsubstituted, or (ii) substituted with one or two  
substituents independently selected from the group

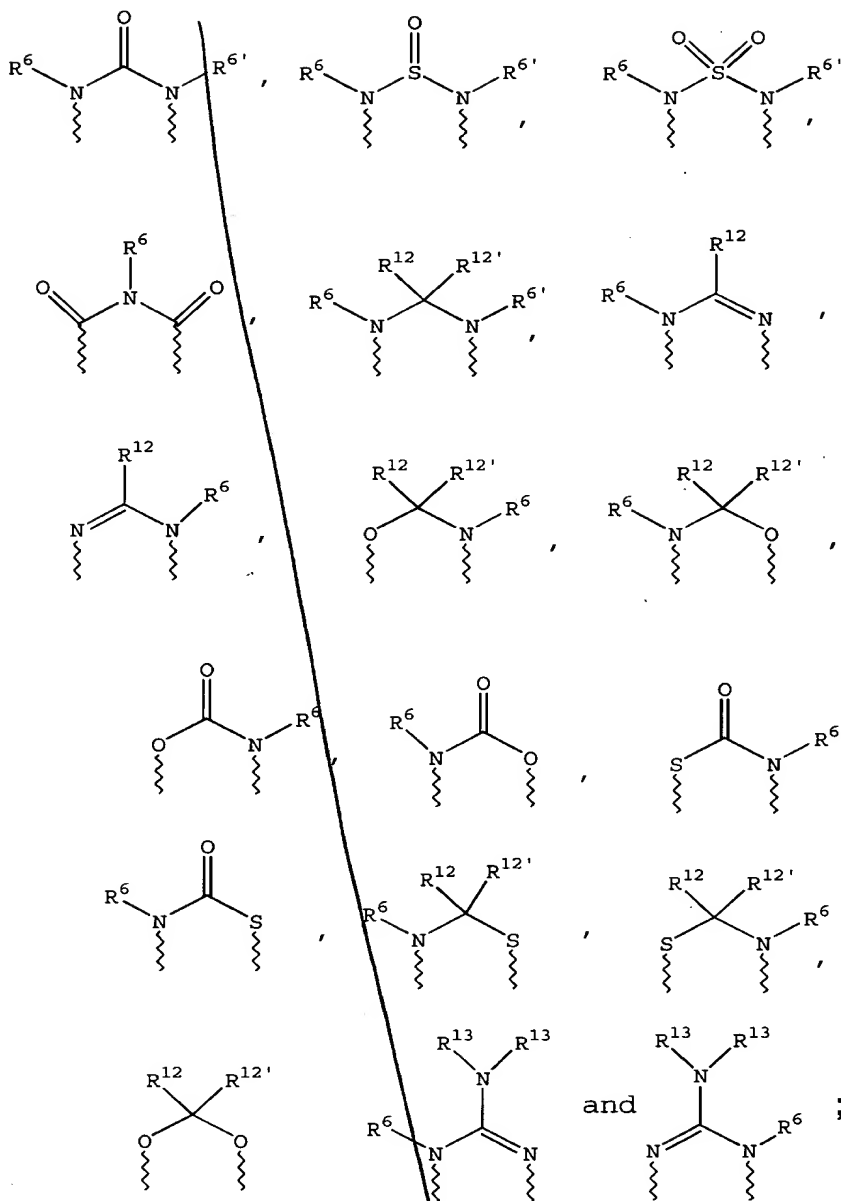
5 membered heterocyclo or heteroaryl ring;

n is zero, 1 or 2;

the sum of  $m + n + p = 1, 2, 3$  or  $4$ ;

(b) X and Z or Z and Y together constitute a moiety that is selected from the group consisting of  $\text{NR}^6\text{C}(\text{O})$ ,  $\text{NR}^6\text{S}(\text{O})$ ,  $\text{NR}^6\text{S}(\text{O})_2$ ,  $\text{NR}^6\text{S}$ ,  $\text{NR}^6\text{O}$ ,  $\text{SS}$ ,  $\text{NR}^6\text{NR}^6$  and  $\text{OC}(\text{O})$ , with the remaining one of X, Y and Z being  $\text{CR}^8\text{R}^9$ , or

(c) n is zero and X, Y and Z together  
20 constitute a moiety selected from the group  
consisting of



5                    wherein wavy lines are bonds to the atoms  
of the depicted ring;

$R^6$  and  $R^{6'}$  are independently selected from  
the group consisting of hydrido, formyl, sulfonic- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkoxycarbonyl- $C_1$ - $C_6$ -alkyl,  
10    hydroxycarbonyl- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -alkylcarbonyl- $C_1$ - $C_6$ -alkyl,  $R^8R^9$ -aminocarbonyl- $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -

- alkoxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl, hydroxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonylcarbonyl, hydroxycarbonylcarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkylcarbonylcarbonyl,
- 5 R<sup>8</sup>R<sup>9</sup>-aminocarbonylcarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkanoyl, aryl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aroyl, bis(C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl)-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-haloalkyl, C<sub>1</sub>-C<sub>6</sub>-perfluoroalkyl, C<sub>1</sub>-C<sub>6</sub>-trifluoromethylalkyl, C<sub>1</sub>-C<sub>6</sub>-perfluoroalkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-
- 10 alkyl, C<sub>3</sub>-C<sub>6</sub>-cycloalkyl, heteroarycarbonyl, heterocyclocarbonyl, C<sub>3</sub>-C<sub>8</sub>-heterocycloalkyl, C<sub>3</sub>-C<sub>8</sub>-heterocycloalkylcarbonyl, aryl, C<sub>5</sub>-C<sub>6</sub>-heterocyclo, C<sub>5</sub>-C<sub>6</sub>-heteroaryl, C<sub>3</sub>-C<sub>8</sub>-cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl,
- 15 heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroarylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, arylsulfonyl, C<sub>1</sub>-C<sub>6</sub>-alkylsulfonyl, C<sub>5</sub>-C<sub>6</sub>-heteroarylsulfonyl, carboxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>4</sub>-alkoxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aminocarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkyl(R<sup>8</sup>N)iminocarbonyl, aryl(R<sup>8</sup>N)iminocarbonyl, C<sub>5</sub>-
- 20 C<sub>6</sub>-heterocyclo(R<sup>8</sup>N)iminocarbonyl, arylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, arylthio-C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>1</sub>-C<sub>4</sub>-alkylthio-C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>5</sub>-C<sub>6</sub>-heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkyl, halo-C<sub>1</sub>-C<sub>6</sub>-alkanoyl, hydroxy-C<sub>1</sub>-C<sub>6</sub>-alkanoyl, thiol-C<sub>1</sub>-C<sub>6</sub>-alkanoyl, C<sub>3</sub>-C<sub>6</sub>-alkenyl,
- 25 C<sub>3</sub>-C<sub>6</sub>-alkynyl, C<sub>1</sub>-C<sub>4</sub>-alkoxy-C<sub>1</sub>-C<sub>4</sub>-alkyl, C<sub>1</sub>-C<sub>5</sub>-alkoxycarbonyl, aryloxycarbonyl, NR<sup>8</sup>R<sup>9</sup>-(R<sup>8</sup>)iminomethyl, NR<sup>8</sup>R<sup>9</sup>-C<sub>1</sub>-C<sub>5</sub>-alkylcarbonyl, hydroxy-

C<sub>1</sub>-C<sub>5</sub>-alkyl, R<sup>8</sup>R<sup>9</sup>-aminocarbonyl, R<sup>8</sup>R<sup>9</sup>-aminocarbonyl-  
C<sub>1</sub>-C<sub>6</sub>-alkylcarbonyl, hydroxyaminocarbonyl, R<sup>8</sup>R<sup>9</sup>-  
aminosulfonyl, R<sup>8</sup>R<sup>9</sup>-aminosulfon-C<sub>1</sub>-C<sub>6</sub>-alkyl, R<sup>8</sup>R<sup>9</sup>-  
amino-C<sub>1</sub>-C<sub>6</sub>-alkylsulfonyl and an R<sup>8</sup>R<sup>9</sup>-amino-C<sub>1</sub>-C<sub>6</sub>-  
5 alkyl group;

R<sup>7</sup> is selected from the group consisting of  
a arylalkyl, aryl, heteroaryl, heterocyclo, C<sub>1</sub>-C<sub>6</sub>-  
alkyl, C<sub>3</sub>-C<sub>6</sub>-alkynyl, C<sub>3</sub>-C<sub>6</sub>-alkenyl, C<sub>1</sub>-C<sub>6</sub>-  
carboxyalkyl and a C<sub>1</sub>-C<sub>6</sub>-hydroxyalkyl group;

10 R<sup>8</sup> and R<sup>9</sup> and R<sup>10</sup> and R<sup>11</sup> are independently  
selected from the group consisting of a hydrido,  
hydroxy, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkanoyl, aroyl, aryl,  
ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryl, heteroar-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>2</sub>-  
C<sub>6</sub>-alkynyl, C<sub>2</sub>-C<sub>6</sub>-alkenyl, thiol-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-  
15 alkylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, cycloalkyl, cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-  
alkyl, heterocycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-  
C<sub>6</sub>-alkyl, aralkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-  
alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxy-C<sub>1</sub>-C<sub>6</sub>-alkyl,  
hydroxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxycarbonylar-C<sub>1</sub>-C<sub>6</sub>-  
20 alkyl, aminocarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-  
alkyl, heteroaryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, arylthio-C<sub>1</sub>-C<sub>6</sub>-  
alkyl, heteroarylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, the sulfoxide or  
sulfone of any said thio substituents, perfluoro-C<sub>1</sub>-  
C<sub>6</sub>-alkyl, trifluoromethyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, halo-C<sub>1</sub>-C<sub>6</sub>-  
25 alkyl, alkoxycarbonylamino-C<sub>1</sub>-C<sub>6</sub>-alkyl and an amino-  
C<sub>1</sub>-C<sub>6</sub>-alkyl group wherein the aminoalkyl nitrogen is  
(i) unsubstituted or (ii) substituted with one or two



radicals independently selected from the group consisting of C<sub>1</sub>-C<sub>6</sub>-alkyl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, cycloalkyl and C<sub>1</sub>-C<sub>6</sub>-alkanoyl, or wherein R<sup>8</sup> and R<sup>9</sup> or R<sup>10</sup> and R<sup>11</sup> and the carbon to which they are bonded form a carbonyl group, or wherein R<sup>8</sup> and R<sup>9</sup> or R<sup>10</sup> and R<sup>11</sup>, or R<sup>8</sup> and R<sup>10</sup> together with the atoms to which they are bonded form a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclic or heteroaryl ring containing one or two heteroatoms that are nitrogen, oxygen, or sulfur, with the proviso that only one of R<sup>8</sup> and R<sup>9</sup> or R<sup>10</sup> and R<sup>11</sup> is hydroxy;

R<sup>12</sup> and R<sup>12'</sup> are independently selected from the group consisting of a hydrido, C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryl, heteroaralkyl, C<sub>2</sub>-C<sub>6</sub>-alkynyl, C<sub>2</sub>-C<sub>6</sub>-alkenyl, thiol-C<sub>1</sub>-C<sub>6</sub>-alkyl, cycloalkyl, cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, heterocycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, amino-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxycarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, hydroxycarbonylar-C<sub>1</sub>-C<sub>6</sub>-alkyl, aminocarbonyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryloxy-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-alkylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, arylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroarylthio-C<sub>1</sub>-C<sub>6</sub>-alkyl, the sulfoxide or sulfone of any said thio substituents, perfluoro-C<sub>1</sub>-C<sub>6</sub>-alkyl, trifluoromethyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, halo-C<sub>1</sub>-C<sub>6</sub>-alkyl, alkoxycarbonylamino-C<sub>1</sub>-C<sub>6</sub>-alkyl and an amino-C<sub>1</sub>-C<sub>6</sub>-alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii)

substituted with one or two radicals independently selected from the group consisting of C<sub>1</sub>-C<sub>6</sub>-alkyl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, cycloalkyl and C<sub>1</sub>-C<sub>6</sub>-alkanoyl;

R<sup>13</sup> is selected from the group consisting of a hydrido, benzyl, phenyl, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>2</sub>-C<sub>6</sub>-alkynyl, C<sub>2</sub>-C<sub>6</sub>-alkenyl and a C<sub>1</sub>-C<sub>6</sub>-hydroxyalkyl group; and

R<sup>20</sup> is (a) -O-R<sup>21</sup>, wherein R<sup>21</sup> is selected from the group consisting of a hydrido, C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl group and a pharmaceutically acceptable cation, (b) -NH-O-R<sup>22</sup>, wherein R<sup>22</sup> is a selectively removable protecting group such as a 2-tetrahydropyranyl, benzyl, p-methoxybenzyl, carbonyl-C<sub>1</sub>-C<sub>6</sub>-alkoxy, trisubstituted silyl group, an o-nitrophenyl group, and a peptide synthesis resin, wherein the trisubstituted silyl group is substituted with C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, or ar-C<sub>1</sub>-C<sub>6</sub>-alkyl or a mixture thereof, (c) -NH-O-R<sup>14</sup>, where R<sup>14</sup> is hydrido, a pharmaceutically acceptable cation or C(W)R<sup>25</sup> where W is O or S and R<sup>25</sup> is selected from the group consisting of an C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, C<sub>1</sub>-C<sub>6</sub>-alkoxy, heteroaryl-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>3</sub>-C<sub>8</sub>-cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, aryloxy, ar-C<sub>1</sub>-C<sub>6</sub>-alkoxy, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, heteroaryl and amino C<sub>1</sub>-C<sub>6</sub>-alkyl group wherein the amino C<sub>1</sub>-C<sub>6</sub>-alkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two substituents independently selected from the group consisting of an C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>3</sub>-C<sub>8</sub>-cycloalkyl-C<sub>1</sub>-C<sub>6</sub>-alkyl, ar-C<sub>1</sub>-C<sub>6</sub>-alkoxycarbonyl, C<sub>1</sub>-

C<sub>6</sub>-alkoxycarbonyl, and C<sub>1</sub>-C<sub>6</sub>-alkanoyl radical, or  
(iii) wherein the amino C<sub>1</sub>-C<sub>6</sub>-alkyl nitrogen and two  
substituents attached thereto form a 5- to 8-membered  
heterocyclo or heteroaryl ring, or (d) -NR<sup>26</sup>R<sup>27</sup>,

5 where R<sup>26</sup> and R<sup>27</sup> are independently selected from the  
group consisting of a hydrido, C<sub>1</sub>-C<sub>6</sub>-alkyl, amino C<sub>1</sub>-  
C<sub>6</sub>-alkyl, hydroxy C<sub>1</sub>-C<sub>6</sub>-alkyl, aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl  
group, or R<sup>26</sup> and R<sup>27</sup> together with the depicted  
nitrogen atom form a 5- to 8-membered ring containing  
10 zero or one additional heteroatom that is oxygen,  
nitrogen or sulfur.

133. The process according to claim 132  
including the further step of recovering said  
15 product.

134. The process according to claim 132  
wherein R<sup>20</sup> is -NH-O-R<sup>22</sup>, wherein R<sup>22</sup> is a  
selectively removable protecting group.  
20

135. The process according to claim 134  
wherein said selectively removable protecting group  
is selected from the group consisting of a 2-  
tetrahydropyranyl, benzyl, p-  
25 methoxybenzyloxycarbonyl, benzyloxycarbonyl, C<sub>1</sub>-C<sub>6</sub>-  
alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>-alkoxy-CH<sub>2</sub>- , C<sub>1</sub>-C<sub>6</sub>-alkoxy-C<sub>1</sub>-  
C<sub>6</sub>-alkoxy-CH<sub>2</sub>- , an o-nitrophenyl group and a peptide  
synthesis resin.

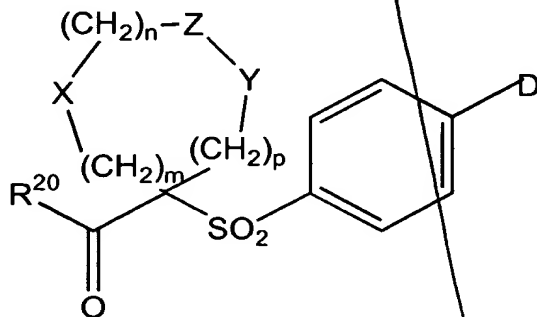
136. The process according to claim 132 wherein said coupling substituent is a nucleophilically displaceable leaving group

5 137. The process according to claim 132 wherein said nucleophilically displaceable leaving group is selected from the group consisting of a halo, nitro, azido, phenylsulfoxido, aryloxy, C<sub>1</sub>-C<sub>6</sub>-alkoxy, a C<sub>1</sub>-C<sub>6</sub>-alkylsulfonate or arylsulfonate group  
10 and a trisubstituted ammonium group in which the three substituents are independently aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl or C<sub>1</sub>-C<sub>6</sub>-alkyl.

138. The process according to claim 132  
15 wherein g is 2.

139. The process according to claim 132 wherein said R<sup>3</sup> is an aryl or heteroaryl group.

20 140. The process according to claim 132 wherein said intermediate that corresponds in structure to formula VI corresponds in structure to formula VIIA, below,



VIIA

wherein D is said nucleophilically  
displaceable leaving group and is selected from the  
group consisting of a halo, nitro, azido,  
phenylsulfoxido, aryloxy, C<sub>1</sub>-C<sub>6</sub>-alkoxy, a C<sub>1</sub>-C<sub>6</sub>-  
5 alkylsulfonate or arylsulfonate group and a  
trisubstituted ammonium group in which the three  
substituents are independently aryl, ar-C<sub>1</sub>-C<sub>6</sub>-alkyl  
or C<sub>1</sub>-C<sub>6</sub>-alkyl.

10 141. The process according to claim 132  
including the further step of recovering said  
product.

15 142. The process according to claim 132  
including the further step of selectively removing  
said protecting group, R<sup>22</sup>.

20 143. The process according to claim 142  
wherein said protecting group, R<sup>22</sup>, is removed after  
carrying out the further step of recovering said  
product.

25 144. The process according to claim 143  
wherein said protecting group, R<sup>22</sup>, is a  
2-tetrahydropyranyl group.

30 145. The process according to claim 133  
wherein R<sup>21</sup> in said product after recovery is  
hydrido, and including the further step of reacting  
said product with hydroxyl amine or a hydroxyl amine  
whose oxygen is reacted with a selectively removable

146. The process according to claim 145  
10 including the further step of recovering the product  
formed.

add 13<sup>18</sup>